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CEREBRAL INJURIES DUE TO EXPLOSION WAVES— "CEREBRAL BLAST CONCUSSION"

A Pathologic, Clinical and Electroencephalographic Study

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THE CONDITION known generically in World War II as "blast concussion," [1] and discussed under synonymous titles by Fulton,[2] Pollock,[3] Fabing,[4] Aita and Kerman [5] and others, is presented here from the point of view of the organic basis of the syndrome. The first case to be described, which is one of the few of its type in which autopsy observations are on record, exemplifies the cardinal factors in this syndrome. These factors can be simplified as follows: One or more nearby explosions, causing no overt or external harm to the skull, nevertheless render the subject unconscious. After this, he has a retrograde amnesia for all but the flash of the explosion, and thereafter anterograde amnesia for a variable period. During this time he may have great motor unrest and normal or exaggerated responses

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1. For a complete review of the literature and bibliography on "Blast Concussion," the reader is referred to the "Clinical History of the Medical Department, United States Army in World War II," to be published by the Department of the Army , Surgeon General's Office.

2. Fulton, J.: Blast Concussion in the Present War, New England J. Med. **226**:1-8 (Jan. 1) 1942.

3. Pollock, L. J.: Blast Injuries of the Central Nervous System, Illinois M. J. **83**:165-168 (March) 1943.

4. Fabing, H.: Cerebral Blast Syndrome in Combat Soldiers, Arch. Neurol. & Psychiat. **57**:14-57 (Jan.) 1947.

5. Aita, J. A., and Kerman, W. Z.: The Closed Head Injury Syndrome Due to Blast, Bull. U. S. Army M. Dept. **6**:411-427 (Oct.) 1946.

to stimuli. On regaining consciousness, he has intense and intractable headache, which later gives way to a milder, but constant, headache; tinnitus; intolerance of noises; tremors, and "nervousness." The last symptom partakes of a variety of types and is usually described in psychiatric terms. "Anxiety" is manifest, and "depression" and "regression" are often employed to describe the dejection and muteness which characterize the behavior of the victim. Neurologic examination is, for the most part, "negative"; i. e., routine observation reveals no signs of gross and lasting damage to major tracts and nuclei within the brain and spinal cord. There are seldom severe paralyses or permanent and unequivocal alterations in reflexes. The evidences of morbidity of the central nervous system are therefore usually interpreted as "functional" or "hysterical."

TERMINOLOGY AND DEFINITION

We have elected to use the term "cerebral blast concussion" in our paper because of the general use of the term and despite the fact that there is no unanimity of definition of the term "concussion" as applied to the brain. At present, it is rather generally agreed that the trauma to the cerebrum comprehended by that term may vary from true "commotio cerebri," or "shaking up" of the brain cells, to a condition of multiple petechial hemorrhages of the brain or to actual contusion. This phase of the general problem of closed head injuries were considered in detail by Symonds,[6] Hassin[7] and Windle and Groat and their co-workers.[8]

The term "blast," as used here, refers to the shock wave: the wave of intensely positive pressure produced by a high explosive. The latter is one which is *brisant,* or capable of blowing to bits all the matter immediately surrounding the detonation itself. We shall consider its effects just outside the area which is called the "zone of brisance," within which everything is disintegrated. Just beyond that zone the shock wave has great traumatic effectiveness, but soon thereafter it loses its force and becomes merely a sound wave. There are many factors which determine the effects of such a wave,

6. Symonds, C. P.: Concussion and Contusion of the Brain and Their Sequelae, in Brock, S.: Injuries of the Skull, Brain and Spinal Cord, Baltimore, Williams & Wilkins Company, 1940, pp. 69-111.

7. Hassin, G. B.: General Pathological Considerations in Brain Injury, in Brock, S.: Injuries of the Brain and Spinal Cord, Baltimore, Williams & Wilkins Company, 1940, pp. 13-40.

8. Windle, W. F.; Groat, R. A., and Fox, C. A.: Experimental Structural Alterations in the Brain During and After Concussion, Surg., Gynec. & Obst. **79**:561-572 (Dec.) 1944. Groat, R. A.; Magoun, H. W.; Dey, F. L., and Windle, W. F.: Functional Alterations in Motor and Supranuclear Mechanisms in Experimental Concussion, Am. J. Physiol. **141**:117-127 (March) 1944. Windle, W. F., and Groat, R. A.: Disappearance of Nerve Cells After Concussion, Anat. Rec. **93**:201-209 (Oct.) 1945.

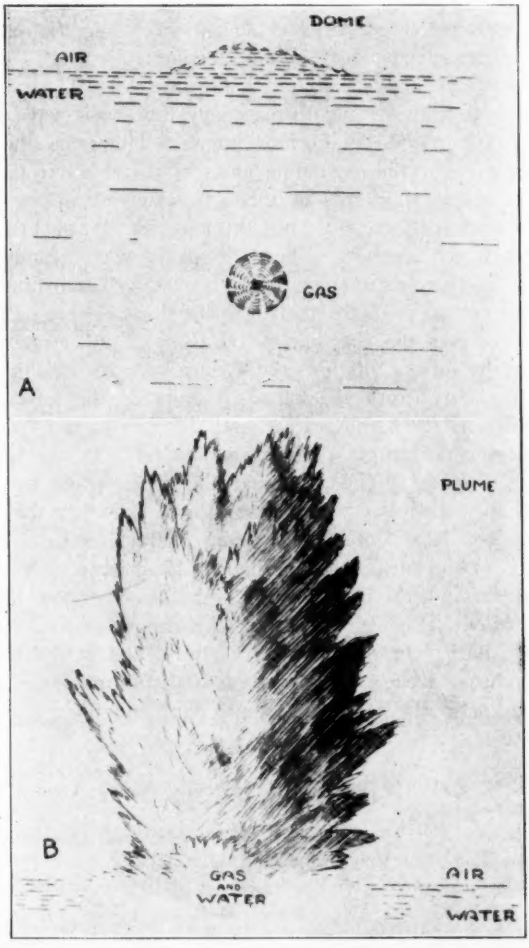

Fig. 1.—*A*, effects of an underwater explosion. The shock wave travels through fluid at nearly 5,000 (1,500 meters) feet per second. At the surface of fluid and gas, disruption of the particles occurs. In the human body, shock is transmitted through the integument, and then through the solid and fluid portions of the body, according to definite physical principles. On surfaces within the gas-bearing structures, i. e., the alveoli of the lungs and the lumen of the intestine, the greatest damage is found. Hemorrhages also occur in other organs. The greatest damage occurs to parts most directly exposed to the shock wave.

B,[13] "plume" resulting from an underwater explosion. This is merely the mixture of gases and water thrown up turbulently after the shock wave has passed. Like the rush of wind which follows an explosion in air, it may hurl about objects in its path, causing secondary damage. The preceding shock wave produces the primary trauma in cases of blast injuries.

and these were considered in detail by Bernal,[9] Robinson,[10] Sutherland,[11] Corey [12] and Wakeley,[13] as well as others. For our purposes, the following epitome suffices: The shock wave has the characteristic of passing through the surrounding mediums at speeds which vary indirectly with the compressibility of the medium. The particles constituting the medium are not displaced by the shock wave itself; they merely oscillate about equilibrium points. However, they may be greatly displaced by the expanding gases which result from the explosion. The shock wave passes through water at nearly 5,000 feet (1,500 meters) per second and through air at about 1,200 feet (360 meters) per second. When the shock wave passes from one medium to another, its rate of speed is changed accordingly, and at the junction of two mediums there may be displacement of the surface particles. For example, the shock wave from an underwater explosion, on reaching the surface, disrupts the surface particles, raising a "dome." This occurs long before the actual passage of the gases generated by the explosion reach the surface and there raise the "plume": the striking, geyser-like eruption of gas and water. In the human body similar effects occur. Thus, whether the shock wave is transmitted to the body through the air, i. e., "atmospheric blast," or through water, i. e., "immersion blast," one of the prime characteristics of the trauma is disruption of the surfaces of the hollow, air-containing viscera. The blast passes through the body mediums, the blood stream, for example, as a shock wave, in contradistinction to a propulsion, or retropulsion, of the blood itself. In the pulmonary alveoli and in the intestine the trauma produces surface hemorrhages, and trauma and hemorrhage may also result in the brain and spinal cord and their linings and in other viscera.[14]

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9. Bernal, J. D.: The Physics of Air Raids, Nature, London **147**:594-596 (May 17) 1941.

10. Robinson, C. S.: Explosions: Their Anatomy and Destructiveness, New York, McGraw-Hill Book Company, Inc., 1944.

11. Sutherland, G. A.: The Physics of Blast, Lancet **2**:641-642 (Nov. 23) 1940.

12. Corey, E. L.: Medical Aspects of Blast, U. S. Navy M. Bull. **46**:623-651 (May 5) 1946.

13. Wakeley, C. P. G.: Effect of Underwater Explosions on the Human Body, Lancet **1**:715-719 (June 9) 1945.

14. (*a*) Bettington, R. H. B.: Injuries to the Ear Due to Blast, M. J. Australia **2**:210-211 (Aug. 18) 1945. (*b*) Stallard, H. B.: Retinal Detachment: A Series of Seventy-Eight Cases in the Middle East Force, Brit. M. J. **2**:330-333 (Sept. 9) 1944. (*c*) Wilson, J. V.: The Pathology of Closed Injuries to the Chest, ibid. **1**:470-474 (April 17) 1943. (*d*) Gutman, P. E.: Isolated Fractures of the First Rib Associated with Blast Forces, Am. J. Surg. **45**:408-412 (Sept.) 1944. (*e*) Bollinger, O.: Ueber traumatische Spät-Apoplexie, Internat. Beitr. z. wissensch. Med. **2**:457-470, 1891.

CLINICAL REPORT

Most of the cases on which this report is based were those of men evacuated from the front as neuropsychiatric problems. In about half of them the primary diagnosis was "psychoneurosis," further qualified, for example, as "war neurosis" or "conversion hysteria." The diagnosis of chronic subdural hematoma was suspected in a number of cases on the basis of the persistent headache, abnormalities of the reflexes, inequalities of the pupils and, rarely, a shift of the pineal gland to one side of the midline, as seen in roentgenograms. In some cases surgical explorations had ruled out hematoma. For the most part, it was apparent that a psychiatric, interpretative approach had been used during the early observation and diagnosis in most of these cases. There were many obvious reasons that comprehensive and careful neurologic examinations were precluded under the conditions in which the first examinations of the patients were made in the battle zones. In contrast, in our hospital in the Zone of the Interior, patients who were suspected of having sustained organic lesions were examined

TABLE 1.—*Percentage Distribution of Electroencephalographic Abnormalities in Cases of Blast Concussion and in Controls*

	Electroencephalogram		
	Normal	Borderline	Abnormal
Controls, per cent	68.6	22.2	9.2
Blast concussion, per cent	56.5	27.6	15.9

as carefully as though one were searching, for example, for lateralizing and localizing signs of cerebral tumor. A statistical study of all the clinical material in the category of closed head injuries treated in this neuropsychiatric and neurosurgical center cannot be given at the present time because of circumstances beyond our control. The incidences of the various types of craniocerebral injuries in which electroencephalographic study was performed are presented in table 1.

The small series for which the findings are given here serve as a prototype for the entire group. Special neurosurgical evaluation was given them, and they represent a sampling over a period of about twenty months of cases in which the patterns of the type of injury, the early and late clinical course and the neurologic findings were essentially the same. The selection of cases for this study was made from those in which direct trauma to the head, either from a missile or blunt blow or from gross acceleration and sudden deceleration of the head, could be ruled out with as much certainty as can be brought into a clinical problem of this type.

Causes of Trauma.—The explosive missiles were mortar shells in about one fourth of the cases, and in the remainder they were artillery

shells of our own and enemy origin, and aerial bombs. Most of the soldiers had some sort of protection by trenches. Several of them, exposed to blasts from heavy shells, estimated that they were within the lethal range of that type of shell. Some said that they were within 50 to 150 feet (16.6 to 50 meters) of exploding 155 mm. shells. In about one third of the cases there were other soldiers within the same hole or slit trench, or in the same immediate site, who either were killed outright by the blast or were injured by it (rather than by shell fragments or debris).

Early Symptoms.—Unconsciousness, headache, tinnitus, dizziness, tremors, symptoms of "nervousness," insomnia and battle dreams and intolerance of noises were the first symptoms.

Unconsciousness: The unconsciousness was usually immediate, but in a few cases it was delayed for a matter of moments or minutes. In the latter case, the neurologic picture, both early and late, was significant of cerebral hemorrhage. In about 20 per cent of the cases the duration of unconsciousness was less than thirty minutes, in about 60 per cent from nine to eighteen hours and in the remaining 20 per cent from two to five days.

Headache: The patient's first awareness after regaining consciousness was usually that of an extremely severe, "bursting" type of headache, which continued unabated from a number of days up to a few weeks before it began to remit to any notable degree. It did not respond to analgesics, and time alone seemed to be the chief leaven.

Tinnitus: This symptom was almost invariable, but was not so intolerable as some of the others.

Dizziness: This symptom, frequently described in terms of true vertigo, had about the same frequency and course as the tinnitus.

Tremor: Tremor took various forms and occurred in about one-half the cases. Usually, it consisted of violent involuntary trembling of all the extremities and the body, but in a few instances it was monolateral, or confined to one arm, in which case the corresponding side of the face was also involved. Occasionally, the tremors were confined to the head. Purposive movements sometimes occurred, and in 1 case a facial motor tic was present.

"Nervous" Symptoms: "Nervousness" was the term most patients used to describe their other symptoms, of which the most frequent was the inability to tolerate loud noises or sudden movements; these stimuli sometimes precipitated strong startle responses. Restlessness and anxiety were described, and fearfulness was frequent, either spontaneous or in response to stimuli, such as the explosion of a shell or the passage of aircraft. Some patients were wildly disoriented and fearful during the early phases and required heavy sedation, which, of course, contributed to many of the cases of prolonged amnesia.

Neurogenic Symptoms: Anesthesia or paralysis occurred not infrequently. Such disturbances were usually transient and were of various types: quadriplegic, hemiplegic and monoplegic.

Insomnia and Battle Dreams: These were frequently complained of.

Late Symptoms.—Headache: The severe headaches usually did not persist without surcease longer than from one to four weeks, this duration obtaining in about 60 per cent of cases. In about 20 per cent of the cases the headache continued as severe and unremitting, and essentially unrelieved by medication, for three months or longer. In another 20 per cent the headache persisted but was relieved at times spontaneously and at other times with medication. No constant reference to changes in the quality or location of the headache could be elicited with respect to alteration in the position of the head, although this played a part in some cases.

Nervous Symptoms: 1. "Nervousness" was complained of by most of the patients, but it was difficult for them to elucidate this symptom further. 2. The inability to tolerate sudden or loud noises was next in severity. 3. About one-fourth the patients stated that they could not tolerate the excitement of social gatherings, that they lost their equanimity and had to forgo such events. On these patients, and on some others, arguments and discussions had a similar effect. They became acutely uncomfortable, in friendly discussions, as well as in serious or contentious ones, and had to leave the vicinity. 4. "Dizziness" partook of the characteristics of true vertigo in less than 10 per cent of the cases. In others momentary periods of feeling dazed or "light" were described.

Effect of Treatment.—For the most part, no specific treatment other than symptomatic treatment and brief psychotherapy had been given these patients. A few had had narcosynthesis during the acute and subacute periods and expressed the opinion that it had given them some relief, but not sufficient to permit them to return to duty.

Physical Examination.—In the late phases, during which we observed these patients, despite the anxiety and dejection which still colored their emotional behavior, an unusually cooperative, relatively dispassionate and objective bearing was observed under the routine conditions of examination. The attitude displayed in case 1, described in detail later, serves as a prototype. The patients who were selected by the neuropsychiatric service for neurosurgical evaluation were examined critically, inasmuch as some were suspected of harboring expanding lesions. For the most part, gross neurologic discrepancies did not persist. Slightly more than one-third the patients still displayed some tremor, usually fine and rhythmic, occasionally of a coarser type and most often involving the extremities on the side on which there was slight hyperreflexia. The head and face were involved only infre-

quently. About 25 per cent displayed slight, but definite and persistent, inequalities in the deep reflexes on the respective sides of the body, one side having hyperreflexia. In slightly less than 50 per cent one pupil appeared consistently larger than the other on repeated observation. However, the pupillary inequality occurred more frequently than the inequality of the reflexes and was observed as often on the right side as on the left. When both conditions were found in the same patient, they were more often contralateral than ipsilateral. This was one of the factors leading to the request for neurosurgical consultation, being, as is well known, one of the signs indicative of chronic subdural hematoma. In the earlier course of our collaboration, pneumoencephalographic examinations were being carried out on these patients. No evidence of subdural hematoma was encountered, but there was usually a visible and measurable enlargement of one of the lateral ventricles. This was almost always on the side opposite the hyperreflexia. It was interpreted by us as evidence of a slight cerebral atrophy, superseding the acute edema and encephalopathy of the trauma.

PATHOLOGIC CHANGES ASSOCIATED WITH BLAST CONCUSSION

REPORT OF A CASE

Cerebral concussion due to nearby mortar shell blast. Prolonged unconsciousness and amnesia. Post-traumatic headache, dizziness, irritability and intolerance to noises. Death three months later, of delayed post-traumatic cerebral hemorrhage from an area of post-traumatic encephalomalacia due to blast injury.

History.—An American private soldier, white, aged 24, a native of Massachusetts, was admitted to a general Army hospital on Feb. 9, 1943, after transfer through a chain of evacuating hospitals, with the transfer diagnosis of "psychoneurosis, war neurosis."

While in battle in Guadalcanal three months previously, in November 1942, the patient was lying prone in a shallow trench when an enemy mortar shell exploded nearby, rendering him unconscious. He was later unable to gage the distance of the explosion exactly but stated the belief that it was "a few feet away." He was taken to a hospital by litter and was told that he was unconscious for eight hours. According to his own statement, he remained dazed and amnesic for the next two weeks. The hospital records indicated that there was no sign of external injury to the head or elsewhere. During this period he took nourishment, attended to his physical needs, was restless and complained frequently.

About one week after the trauma he was removed to a base hospital, where he remained six weeks. He complained of headache, dizziness, tinnitus and irritability to noises. He was described as being depressed, with diminished affect and tremor of his hands. There were noted occasional unsteadiness of gait and past pointing in the finger to nose test. Medication afforded him essentially no relief from his headache, which remained extremely severe for about six weeks. It was apparent from the hospital record that the patient's symptoms were interpreted as of functional origin.

His complaints remained essentially unchanged in quality on his admission to the neuropsychiatric service of the general hospital except that the headache was no longer as severe as it had been for the first several weeks. He appeared well nourished, was somewhat restless and tense but mingled freely with the other patients and participated in various recreational activities of the hospital. Psychiatric examination did not reveal any personal determinants indicating a psychoneurosis. He continued to complain of headaches, but his tension subsided considerably.

On February 12, three days after admission, while straining at stool, he had a sudden, extremely severe pain "in the temporal region" (side not specified), which became gradually, progressively and relentlessly worse. He had extremely severe nuchal pain and vomited several times. Neurologic examination revealed nuchal rigidity and Kernig's sign, apathy and restless somnolence. The deep reflexes were slightly stronger on the left side, with the biceps jerk spreading to the fingers, and Hoffmann's sign was elicited. Plantar flexion was normal on the left, but there was fanning of the toes on the right. There was drooping of the left side of the face.

Chemical and cytologic studies of the blood and urine gave normal results. The cerebrospinal fluid was grossly and uniformly bloody.

Except for restlessness and emotional response to his pain, and the display of some annoyance when the neurosurgeon attempted to elicit a detailed history of the trauma and the subsequent course leading up to his recent acute complication, the patient's mental attitude and emotional state were normal. He was loath to talk about his condition, his explanation being that he felt himself to have been misbelieved when he had been interrogated at various times in the past. Asked to state his chief complaint in his own words, he stated: "I don't 'complain,' sir. But only since you insist: I have had constant headache and dizziness since I recovered consciousness, and treatment has given me no relief. I have been told that I am psychoneurotic and that my complaints arise from my mind. I am not competent to discuss a medical diagnosis, but to me my complaints have been very real. The headache I have now is new and different from the one I had before. I don't care what the diagnosis is, as long as I get some relief."

This patient grew progressively and sporadically worse, with crises of slow pulse, syncope and excruciating headache. He was seen in neurosurgical consultation because the persistence of severe headache since the onset of his illness made it desirable to rule out the possibility of subdural hematoma.

Operation.—This etiologic possibility seemed slight; but, because of the urgency of his present condition, bilateral trephine explorations were carried out in the early morning. These trephinations revealed only blood in the subarachnoid space, with increased cerebral tension and edema of the cortex. His condition continued to be progressively worse, and he became apathetic and febrile; the pupils became fixed, irregular and dilated, the left being larger than the right. Cheyne-Stokes breathing supervened; the pulse was rapid and thready; apnea developed, and he died the next day.

Diagnosis.—The clinical diagnosis was: (1) ruptured congenital aneurysm in a case of cerebral blast concussion or (2) cerebral blast concussion with delayed post-traumatic hemorrhage (*Spät-Apoplexie* [14e]).

Autopsy.—Gross Pathologic Study: (*a*) Skull: Except for the bilateral trephine openings in the posterior portion, the skull and dura mater were normal.

(*b*) Leptomeninges: The leptomeninges were normal; the subarachnoid space contained hemorrhage, chiefly around the pons and brain stem.

(*c*) Brain: The brain weighed 1,280 Gm. The sulci were slightly flattened. There were no congenital aneurysms or varices. The basilar vessels showed no evidence of injury or arteriosclerosis. Section of the brain after fixation revealed a massive hemorrhage involving and destroying the posterior part of the internal capsule, the caudate nucleus and parts of the thalamus on the left side. The hemorrhage had perforated into the lateral ventricle. The tissue surrounding the hemorrhage was of soft consistency and grayish brown and contained numerous small hemorrhages. The point of the bleeding vessels could not be determined. The brain tissue of the right hemisphere was edematous.

(*d*) Spinal cord: The cervical portion of the spinal cord, which was removed with the brain, showed no gross pathologic change.

Microscopic Pathologic Studies: (*a*) Acute changes: At the site of the lesion there was massive hemorrhage with extensive destruction of the brain tissue and numerous secondary hemorrhages. Other sections of the brain showed diffuse edema and an occasional thrombosed vein, which was greatly dilated.

(*b*) Chronic changes: The tissue adjacent to the hemorrhage showed severe myelin degeneration with beginning gliosis and some hemosiderin. The ependymal lining was intact, but there were subependymal gliosis and edema. Sections of the cerebellum showed no pathologic changes.

Summary.—The pathologic report (Major Emmerich von Haam) was as follows:

"The death of the patient was due to a severe intracerebral hemorrhage with increased intracranial pressure and extensive destruction of brain tissue. The age of the patient and the normal appearance of the entire arterial system, including the basilar artery and its branches, make the diagnosis of arteriosclerosis and syphilitic or mycotic arteritis improbable. No miliary aneurysms were seen anywhere, and the clinical history suggests some relation of the hemorrhage to the blast injury the patient sustained in the Pacific war area."

The final pathologic diagnoses were: (*a*) severe intraventricular hemorrhage, and (*b*) extensive subacute, traumatic encephalomalacia, due to blast concussion.

COMMENT

Most of the reports of "blast injury" in the literature[15] deal with injuries to the abdominal and thoracic viscera. In these cases of severe injury, the mental disturbances and the lesions in the brain are often commented on only incidentally.

Grinker and Spiegel,[16] in discussing cases of concussion in which there had been no solid blow to the skull, described 2 instances of delayed post-traumatic hemorrhage which had come to their attention. The patients had had symptoms "persisting for several weeks after their battle experiences," consisting of anxiety, insomnia and restlessness. The first of these 2 patients died after a sudden fall to the ground, fracturing his skull and rupturing a meningeal blood vessel. Autopsy revealed old hemorrhages within a severe laceration of the frontal lobe. The second patient had severe frontal headache, then

15. Zuckerman, S.: Problem of Blast Injuries, Lancet **1**:110-118 (Jan. 25) 1941. Fearnley, G. R.: Blast Injuries to the Lungs: Clinical and Radiological Findings and Their Relation to Certain Symptoms, Brit. M. J. **1**:474-477 (April 7) 1945.

16. Grinker, R. R., and Spiegel, J. P.: War Neuroses in North Africa: The Tunisian Campaign, New York, Josiah Macy Jr. Foundation, 1943.

coma, and died. Autopsy revealed extensive old injury to the frontal lobes, into which fresh hemorrhages had taken place, causing death. The authors noted that in neither case had adequate neurologic examination been made and that lumbar punctures had not been performed, and stated:

> Perhaps some of our discharged patients with anxiety states die in other hospitals with terminal hemorrhages into lacerated brains. It is unfortunate that follow-up studies cannot be made; yet our opinion is that such cases are infrequent.

Grinker [17] stated the belief that these cases represent blast concussion. Descriptions of other cases of cerebral blast injury were given by Rogers [18]; Ascroft [19]; Bell [20]; Grunnagle [21]; Wood and Sweetzer [22]; Stewart, Russell and Cone [23]; Abbott, Due and Nosik [24]; Hamlin [25]; Ganado,[26] and Cohen and Biskind.[27] The types of pathologic lesions described include cerebral edema, petechial hemorrhages, meningeal hemorrhages, cerebral contusion and laceration, intracerebral hematoma and subdural hematoma.

THE ELECTROENCEPHALOGRAM ASSOCIATED WITH BLAST CONCUSSION

Routine electroencephalograms were obtained in 441 cases in which the clinical diagnosis of "blast concussion" had been made on the basis of the criteria previously enumerated. Unconsciousness had occurred in 329 cases. Positive evidence of blast damage, as demonstrated by bleeding from the ears or nose, rupture of the drum membrane or conjunctival hemorrhages, occurred in 77 cases. In 5 cases convulsive

17. Grinker, R. R.: Personal communication to the authors.

18. Rogers, L.: Blast Injury of the Brain, M. J. Australia **2**:209-210 (Aug. 18) 1945.

19. Ascroft, P. B.: Blast Injury of the Lungs with a Curious Lesion of the Cerebrum, Lancet **1**:234-235 (Feb.) 1943.

20. Bell, R. C.: Analysis of Two Hundred and Fifty-Nine of the Recent Flying Bomb Casualties, Brit. M. J. **2**:689-692 (Nov. 25) 1944.

21. Grunnagle, J. F.: Traumatic Intracerebral Hematoma, paper on file in the Surgeon General's Office.

22. Wood, H., and Sweetzer, H. B.: Punctate Cerebral Hemorrhage Following Thoracic Trauma, U. S. Nav. M. Bull. **46**:51-56 (Jan.) 1946.

23. Stewart, O. W.; Russell, C. K., and Cone, W. V.: Injury to the Central Nervous System by Blast: Observations on a Pheasant, Lancet **1**:172-174 (Feb.) 1941.

24. Abbott, W. D.; Due, F. O., and Nosik, W. A.: Subdural Hematoma and Effusion as a Result of Blast Injuries, J. A. M. A. **121**:664-666 (Feb. 27); 739-741 (March 6) 1943.

25. Hamlin, H.: Symposium on Immersion Blast Injuries, U. S. Nav. M. Bull. **41**:26-32 (Jan.) 1943.

26. Ganado, W.: Blast Injuries, Brit. M. J. **2**:118 (July 24) 1943.

27. Cohen, H., and Biskind, G.: Pathologic Aspects of Atmospheric Blast Injuries in Man, Arch. Path. **42**:12-34 (July) 1946.

seizures followed exposure to blast, and there was no history of convulsions prior to the injury. In 2 cases included in this series there was a doubtful history of exposure to blast, and in 3 cases the referring medical officer made the diagnosis of psychoneuroses, with questionable exposure to blast injury.

Inasmuch as the patients with milder blast concussion were returned to duty, the patients on whom this study was based were those with more serious concussions, and these studies represent only the late, residual changes. The time elapsed between the injury and the electroencephalographic recording ranged from three weeks, in 1 case, to at least eighty weeks, in 6 cases. The mean time elapsed was 24.4 weeks. The fact that changes in the electroencephalogram persisted so long after trauma emphasizes the probability of real, irreversible traumatic changes occurring in the brains of patients with blast concussion.

ELECTROENCEPHALOGRAPHIC FINDINGS

The electroencephalograms obtained in these cases ranged from entirely normal to pathognomonically abnormal.[28] In figure 2, the distribution of normal, borderline and abnormal electroencephalograms is compared with the distribution in cases of other conditions. The percentage distribution is represented in table 1.

The figures represented in table 1, when subjected to the chi square test, show statistically significant deviation from the normal, with the incidence of borderline and abnormal records obtained from patients subject to blast injury falling well outside the limits of probable chance.

When the electroencephalographic findings are correlated with the histories of loss of consciousness, a seeming paradox appears. In those cases in which there was no loss of consciousness the incidence of borderline and abnormal electroencephalograms was significantly higher than in cases in which there was loss of consciousness. This would appear to be in opposition to the observations of Jasper, Kershman and Elvidge,[29] who found a "small correlation between the length of unconsciousness and the severity of cerebral damage as judged by the initial electroencephalogram." However, their conclusions were based on electroencephalograms taken within ten days of the time of injury, whereas the present series deals only with those taken long after the injury. No adequate

28. Davis, P. A.: Technique and Evaluation of the Electroencephalogram, J. Neurophysiol. **4**:92-114 (Jan.) 1941. Gibbs, F. A.; Gibbs, E. L., and Lennox, W. G.: Electroencephalographic Classification of Epileptic Patients and Control Subjects, Arch. Neurol. & Psychiat. **50**:111-128 (Aug.) 1943. United States War Department Technical Bulletin (TB Med 74), Electroencephalography: Operative Technique and Interpretation, Bull. U. S. Army M. Dept. **4**:360 (Sept.) 1945.

29. Jasper, H. H.; Kershman, J., and Elvidge, A.: Electroencephalography in Head Injury: Trauma of the Central Nervous System, A. Research Nerv. & Ment. Dis., Proc. (1943) **24**:388-420, 1945.

explanation of this finding in the present series is available other than the persistence of changes resulting from the injury, and indicative of long-lasting alterations in the cortical processes.

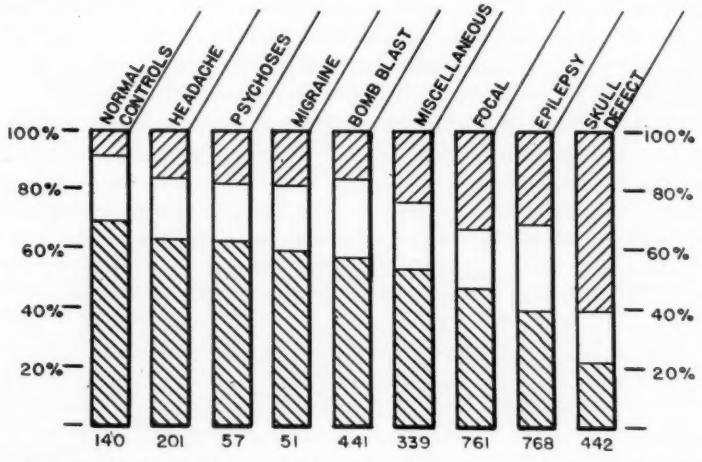

Fig. 2.—Distribution of normal, borderline and abnormal electroencephalograms in eight clinical groups, as compared with the records for normal controls.

In this figure, and in figure 3, the clear rectangles indicate borderline electroencephalograms; rectangles with cross hatching from right to left, abnormal electroencephalograms, and rectangles with cross hatching from left to right, normal electroencephalograms.

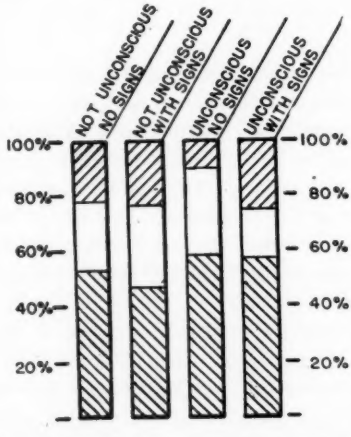

Fig. 3.—Distribution of normal, borderline and abnormal electroencephalograms following bomb blast concussion, with and without unconsciousness and with and without physical signs of blast injury.

On the other hand, in cases in which positive physical signs of blast trauma were present, there was definitely more electroencephalographic abnormality than in cases without physical signs. These findings are illustrated in figure 3.

The 5 doubtul cases and the 5 cases in which convulsive seizures followed blast injury are not included in figure 3. In 2 of the cases with convulsions the electroencephalograms showed borderline abnormalities, and in 3 they were definitely abnormal. In 1 case with repeated seizures localized spikes arose from the left premotor area. Since the pneumoencephalogram showed no abnormality indicating need for surgical intervention, no operative procedure was undertaken.

In the present series there was noted an increase in the incidence of intermediate activity [30] of 13 to 18 cycles per second. The percentage incidence of blast concussion, as compared with that for closed head injury, open head injury (skull defect and depressed fractures) and normal controls, is shown in the following tabulation.

Blast Concussion	Closed Head Injury	Open Head Injury	Normal Controls	All Other Conditions
27.7%	26.6%	23.1%	20.0%	23.3%

TABLE 2.—*Incidence of "Double Alpha" and of Suppression of Alpha Rhythm in Various Cerebral Disorders*

Series	Number	Incidence of "Double Alpha," Percentage	Incidence of Suppression of Alpha, Percentage
Bomb blast	441	9.1	6.6
Controls	140	6.4	2.1
Epilepsy	768	4.5	3.9
Focal lesion	761	6.7	10.7
Migraine	51	5.9	2.0
Headache	201	4.5	2.0
Skull defects	442	5.7	24.7
Psychoses	57	5.3	5.3
Miscellaneous	339	4.7	2.6

Although these figures are not statistically significant, they closely approach the borderline and appear to indicate a trend toward abnormal activity. A larger group of control cases, with the same percentage incidence, would render the findings definitely significant. The close agreement between the incidence for blast concussion and that for closed head injury confirms the impression gained in the laboratory that blast concussion is, at least electroencephalographically, only a subdivision of the greater group of closed head injuries, including concussion from any source.

There was also noted a moderate increase in the incidence of disruption of the alpha activity to twice its frequency, giving rise to the occurrence of "double alpha." The increase in this characteristic is not sufficient to warrant the assumption of any definite conclusions, but it, again, represents a trend.

Suppression of alpha activity occurred significantly oftener in the electroencephalograms of patients with blast concussions than in those of normal subjects. It was found oftener in cases of closed injury

30. Brazier, M. A. B., and Finesinger, J.: Characteristics of the Normal Electroencephalogram, J. Clin. Investigation **23**:303-311 (May) 1944.

and oftenest in cases of very severe skull defects. Williams and Reynell [31] stated the belief that this suppression of the alpha rhythm is "always abnormal" and found it occurring "around penetrating gunshot wounds of the brain, . . in the cortex underlying nonpenetrating gunshot wounds, and depressed fractures, and in other circumstances in which the brain is violently percussed." Again, the evidence in this series points toward definite damage to the brain. The incidence of "double alpha" and of suppression of alpha activity is shown in table 2.

COMMENT

The electroencephalograms of 441 patients who were exposed to blast concussion showed a significantly higher incidence of borderline and abnormal tracings than was found in a smaller group (140) of control subjects. Suppression of alpha activity in these records had likewise a significant incidence. In addition, there were found increased intermediate activity and "double alpha," though the incidence of frequencies was not statistically meaningful. These characteristics, taken together, however, indicate with reasonable probability that there was residual cerebral damage in these cases. The persistence of abnormalities as long as two years after the injury, with a mean duration of three months, also lends emphasis to the probability that severe damage was present in many cases. Since many of the men subjected to blast concussion were soon returned to duty, the over-all incidence of persistent trauma was presumably considerably lower than that among these patients with severer concussion who were transferred to the general hospital.

Garai [32] observed a patient with cerebral blast injury (not a typical case of blast concussion, but one in which the neurologic changes would lead to the diagnosis of a contusion) and compared the electroencephalograms taken during the first days and weeks after the trauma with those obtained one year later. Although the changes in the latter were no longer so pronounced, the general character of the dominant rhythm had remained unchanged, there being generalized irregularity with a tendency to slow frequencies. Garai concluded that the following factors were in favor of an acquired dysrhythmia in his case (bearing in mind that 10 per cent of the normal population have abnormal rhythms): (1) asymmetry of the rhythm in the two hemispheres; (2) a change in the rhythms in the course of time.

31. Williams, D., and Reynell, J.: Abnormal Suppression of Cortical Frequencies, Brain **68**:123-161 (June) 1945; quoted from Digest Neurol. & Psychiat. Inst. of Living **14**:145, 1946.

32. Garai, O.: Blast Injury: Non-Fatal Case with Neurological Signs, Lancet **1**:788-789 (June 17) 1944.

GENERAL COMMENT

PROOF OF BLAST CONCUSSION

Our observations are consonant with the facts published by others who assert that blast concussion is a definite clinical and pathologic entity. They leave little doubt that its basis is structural, organic, and not purely functional. They strongly suggest that blast concussion is merely one type of cerebral concussion, differing only in the mechanism of its production and in being peculiar to warfare. All those who have come to this opinion as a result of their observations have made a special effort to eliminate cases in which there was possible gross injury to the skull. In von Storch's [33] observations on blast concussion casualties at the front, eye witness corroboration or its equivalent was a criterion for diagnosis. This criterion is admittedly difficult to fulfil, for the effects of the blast are unpredictable, as discussed by Barrow and Rhoads.[34] An illustrative case from our own material concerned three soldiers who were occupying one trench, all facing the enemy's fire. The two men at either end were killed outright by the blast of a shell which exploded in front of them; the soldier in the center was rendered unconscious and after recovery had the typical postconcussional syndrome. Eye witness accounts in the medical literature are few. Tunbridge [35] reported an incident of blast concussion viewed by eye witnesses. Like others who have published work on the subject, we, too, endeavored to obtain independent information regarding the effects of blast by interrogating numerous participants in battle, of all military grades, who had not been injured by blast. Their objective descriptions of the unpredictable effects of blast coincided with the accounts contained in the case histories accompanying the casualties whom we examined in the later periods of recovery. Our informants who were best equipped by natural intellect and education to give an objective and dependable opinion, particularly officers who had served in the closest contact with their men over extended periods, stated that in their measured opinion the breakdown was not primarily psychogenic in those cases of which they knew, in which the men had been evacuated because of blast concussion.

Denny-Brown [36] stated that, in his opinion, the probable mechanism for the production of blast concussion is acceleration of the head

33. von Storch, T. J. C.: A Study of Cerebral Concussion, Annual Report, 33rd General Hospital (U. S.), 1945, on file in the Surgeon General's Office; in discussion on this paper.

34. Barrow, D. W., and Rhoads, H. T.: Blast Concussion Injury, J. A. M. A. **125**:900-902 (July 29) 1944.

35. Tunbridge, R. E.: Cause, Effect and Treatment of Air Blast Injuries, War Med. **7**:3-6 (Jan.) 1945.

36. Denny-Brown, D.: The Effect of High Explosives on the Post-Traumatic Syndrome, Tr. Am. Neurol. A. **69**:98-102, 1943.

of the victim to move through a sufficient arc, at a sufficiently great speed and for a sufficiently long moment of time to have caused the concussion. He decried the attempt to explain it on the basis of other mechanisms. However, Denny-Brown's explanation would not hold for immersion blast concussion of the central nervous system, as in the cases cited by Hamlin.[25] The victims were floating in water, supported by life belts, and there is every probability that the head or body was not accelerated by the shock wave. The latter manifestly created the damage by being transmitted through the walls of the immersed body, and thence through the various body mediums to the other organs. Rowbotham's [37] observations corroborated those of others, namely, that blast may blow the victims to bits, or kill them outright, in the positions and attitudes in which they were when exposed.

PARACRANIAL TRANSMISSION OF THE SHOCK WAVE TO THE CEREBRUM

The data in our case histories ruled out a transcranial application of the forces involved, and the paracranial transmission was postulated by virtue of the concomitant symptoms of pulmonary concussion which some patients had displayed. Furthermore, as we studied this ever recurring syndrome, it became increasingly evident that the residual signs which we saw in the late stages were chiefly of brain stem origin and that the early manifestations were doubtless also due to disturbance from this source. We share with Stewart, Russell and Cone [24] and Hamlin [26] the concept that the percussion wave is applied to the body wall, and that the force is then transmitted as a shock wave by way of the body fluids. More specifically, it traverses the abdominal and thoracic venous lake and is transmitted to the cranium by two routes. The first is by way of the venous lake comprised of the jugular veins, the lateral and longitudinal sinuses, the great cerebral vein (of Galen) and the parasagittal veins, which transmit the shock directly to the substance of the brain. The second is by way of the lake comprised of the spinal veins and the spinal fluid, through which the shock wave is transmitted to the intracranial contents. In this connection, it is to be emphasized that the traumatic force is a shock wave, a transmittal of pressure through fluid, as distinguished from a rush or flow of blood per se. No unusual movement of the mass of the blood stream is envisioned. It is the actual application of intense pressure to the brain cells, as well as on the capillaries, which produces the lesions. We judge the location of the latter to be principally in the nuclear masses surrounding the third and fourth ventricles.

37. Rowbotham, G. F.: Acute Injuries of the Head, Edinburgh, E. & S. Livingston, 1945.

PRODUCTION OF SPECIFIC SYMPTOMS

Unconsciousness.—As illustrated by some of our cases, and by others recorded in the literature, in which the blast produced cerebral hemorrhage,[38] unconsciousness need not occur at all and yet the brain may be obviously damaged. We used unconsciousness as a criterion of concussion, and we attributed it to the concussive effects on the centers of the brain stem controlling sleeping and waking, in the hypothalamus, midbrain and hindbrain, as discussed by Jefferson[39] and Davison and DeMuth.[40] Fabing,[4] who leaned strongly toward a functional basis as against a physical disturbance in the brain, nevertheless pointed out that there is a moment of incontrovertible loss of consciousness which cannot be recalled by the methods of hypnosis and narcosynthesis, whereas the phenomena in the period of amnesia may be recalled. This fact, seen in the light of the work by Windle, Groat and their co-workers,[8] makes it necessary to accept the concept of an organic change as the basis for the unconsciousness and the subsequent symptoms.

Headache.—Headache was intense and persistent in 93 per cent of cases and abated spontaneously in a period of days or weeks. We interpret this symptom as, first, an index of organic disturbance, and not one basically of psychogenic origin. Like the remaining symptoms of somatic type, headache was present in full force with the first moments of returning consciousness. Fabing[4] interpreted this pain as functional. He rejected the suggestion that hemorrhage, which is usually accepted as an evidence of organic injury, plays any part in the production of symptoms in cases of blast concussion. He also stated the belief that because headache was relieved in many cases by chemical hypnosis with "pentothal"—even though all patients were not relieved of headache by this treatment, and many were not cured of it—it, therefore, cannot be properly considered as of "organic" origin. However, the concussion wave places the blood vessels, meninges, bone and periosteum, muscles and integument under stress, and they may not properly be completely eliminated as possible sources of pain. It is true that narcosis, with or without hypnotic suggestion, may well leave a greater or lesser increment of relief, as do many other measures which temporarily interrupt the cycle of a pain-producing mechanism. In cases of blast concussion or encephalopathy, even as of brain tumor, many symptoms are often labeled "psychosis" or "neurosis" until the

38. Grunnagle.[21] Garai.[32]

39. Jefferson, G.: The Neurological Interpretation of the Acute Head Injury, Tr. Am. Neurol. A. **69**:13-16, 1943; The Nature of Concussion, Brit. M. J. **1**:1-5 (Jan. 1) 1944.

40. Davison, C., and DeMuth, E. L.: Disturbances in Sleep Mechanism: A Clinico-Pathologic Study, Arch. Neurol. & Psychiat. **55**:111-125 and 126-138 (Feb.); 364-381 (April) 1946.

diagnosis is established, whereupon they may readily be comprehended as specific symptoms of the organically altered function of the part involved.

Aside from the variety of gross traumatic lesions which doubtless contribute to the headache, it seems to us that a central mechanism may be imputed in the form of cellular changes in the somatic sensory components of the nuclei of the vagus and trigeminal nerves which supply the dura mater; likewise, such lesions may well occur in the thalamus and the dysfunction consequent thereto be experienced as somatic discomfort. In our own case there were gross lesions in the thalamus, and Windle and his co-workers [8a, c] demonstrated the susceptibility to the trauma of concussion of the nuclei of the trigeminal nerve and other sensory nuclei in the brain stem. In Brubaker's [41] cases pain was referred to the forehead in such localized manner that he considered it due to involvement of the ophthalmic division of the trigeminal nerve. Some relief was obtained by deafferentiation with injections of procaine.

Symptoms of Acoustovestibular Type.—Windle and Groat [8c] and Windle, Groat and Fox [8a] described the postconcussive intraneuronal changes in the lateral vestibular nuclei, the medial vestibular and cochlear nuclei and elsewhere in the brain stem in cases of experimental concussion. These observations supported the opinions long held by German writers that the vertigo, and possibly some of the tinnitus, which cannot be ascribed to direct concussion of the primary hearing mechanism may well be due to lesions in the brain stem. We concur in this opinion and further propose that the intolerance to noise has a similar organic basis. Such specific symptoms are usually labeled empirically as "anxiety" symptoms. No doubt these symptoms may occur as a neurosis, just as may many others, without demonstrable disease to account for them. On the other hand, in the group under consideration, neurosis being ruled out, we consider this part of the syndrome as evidence of a basic cellular disturbance in the central nuclei mediating and amplifying hearing and equilibrium.

Abnormal Deep Reflexes and Inequalities of the Pupils.—Persistent inequality of the pupil in many of our cases was not in itself localizing in that one could postulate a lesion at any one point. We attributed such changes to lesions in the midbrain. The inequality of the pupils occurred in 50 per cent. According to Turner,[42] asymptomatic pupillary inequality occurs in 5 to 10 per cent of the general population. The fact that definite alterations in the deep reflexes were not recorded during the acute phases of this condition in the present series in not remark-

41. Brubaker, R. E.: Air Blast Injury: Report of Cases, Bull. U. S. Army M. Dept., 1945, no. 87, pp. 110-114.

42. Turner, E. A.: Pupillary Inequality, Brain **68**:98-117 (June) 1945.

able, for usually only a specialist is keenly interested in demonstrating such small changes and in evaluating them in respect to the probable lesion producing them. Most casual examiners, in our observation, are apt to beg the question when there are only moderate discrepancies. Yet, in our experience in diagnosis and localizations of expanding intracranial lesions, these small signs have often been sufficient in themselves, when all were in consonance, to permit localization on clinical grounds alone. Furthermore, it should be noted in passing that even very large expanding lesions sometimes produce only minimal neurologic changes, and in cases of concussion in general it is not the rule to find outspoken abnormalities of lateralizing or localizing value unless a cerebral contusion and complications thereto exist.

Our personal experience with this problem does not include the acute stages. However, in view of our observations on the late phases of the disturbance, we would caution against the quick interpretation of temporary pareses of limbs, the so-called bizarre gait, changes in reflexes in the extremities and inequality of the pupils of abnormal pupillary reflexes as due to conversion hysteria, merely because they do not fit into the observer's conception of a pattern of organic neurologic disturbance. In the light of our general experience with neurosurgical diseases, and our findings in these cases of the late stage of blast concussion, we are forced to interpret these observations in acute cases as due to generalized and focal small lesions in the brain and the brain stem. In so doing, we bear in mind, however, that the moderate postconcussional, postedematous atrophy of the brain and the progressive intrinsic glial cicatrization which must accompany the healing of cerebral lesions may in themselves produce a late neurologic and electroencephalographic status quite different from the picture observed in the acute phases, irrespective of the obvious difference and influence of the psychic states in the two instances.

SUMMARY

1. The so-called blast syndrome of postconcussional sequelae is presented in the light of a true encephalopathy.

2. An entirely typical clinical case of blast concussion, in which the patient succumbed to a delayed hemorrhage from an area of posttraumatic cerebral softening in the thalamus, is reported, with autopsy.

3. The neurologic aspects of the problem are presented and discussed in respect to the organic origin of symptoms, from diffuse cerebral and localized lesions of the brain stem.

4. The electroencephalographic findings in a series of 441 cases with this clinical diagnosis are discussed, and evidence from the abnormal brain waves is adduced to indicate the organic basis for this condition.

VOCALIZATION AND ARREST OF SPEECH

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IN ORDER to set the stage for a study of aphasia, we record here certain observations in regard to (*a*) vocalization as a response to stimulation of the human cerebral cortex and (*b*) arrest of speech by means of stimulation. We have supplemented these observations with limited reference to the effect of excision of areas of the sensorimotor convolutions in the dominant or the nondominant hemisphere.

VOCALIZATION

In 1935, as the result of using a thyratron physiologic stimulator on the precentral gyrus of a man with local anesthesia, one of us (W. P.) was surprised by a clear, sustained vowel cry. After the electrode was withdrawn, the patient observed that something had made him speak.

Repeated stimulation in a small zone limited to a few millimeters reproduced the sound over and over again. If stimulation was prolonged, it continued until breath was exhausted, whereupon the patient took a breath and continued. This case was reported in some detail, together with 5 subsequent cases of the same phenomenon, in the Harvey Lecture [1] of 1936.

In the first case referred to here, the threshold seemed to be lower for vocalization than for any other motor phenomenon in the precentral gyrus. Consequently, there was no distortion of the face or mouth during phonation and no accompanying cortical sensation. Two discrete points of response were found. The first occupied an area 2 to 3 mm. in diameter; the second was a little less than 1 cm. below on the precentral gyrus, and from it was produced a sound that was lower in pitch.

From the Department of Neurology and Neurosurgery, McGill University, and the Montreal Neurological Institute.

1. Harvey Lecture, delivered before the New York Academy of Medicine, Oct. 15, 1936; later reported, with additions (Penfield, W.: Cerebral Cortex in Man, Arch. Neurol. & Psychiat. **40**:417 [Sept.] 1938) and referred to by Penfield and Boldrey (Brain **60**:389, 1937).

This response was vocalization without words. It was clearly a vowel sound, such as is used in speaking, but it was not the same as the inspiratory or expiratory grunt sometimes obtained. The mouth opened and the tongue held still, but there was in this vocalization no further coordinated movement of the lips and tongue and no interruption of expiratory movement such as is necessary to bring about word utterance.

After the report of these 6 cases, no particular effort was made to elicit such a response. However, the present review of the records of subsequent craniotomies, carried out with local anesthesia, and in which electrical exploration seemed necessary, has added 51 such responses in 29 cases. In figure 1, the points from which vocalization was induced in different cases are placed in summary form on the brain maps of the right and the left hemisphere.

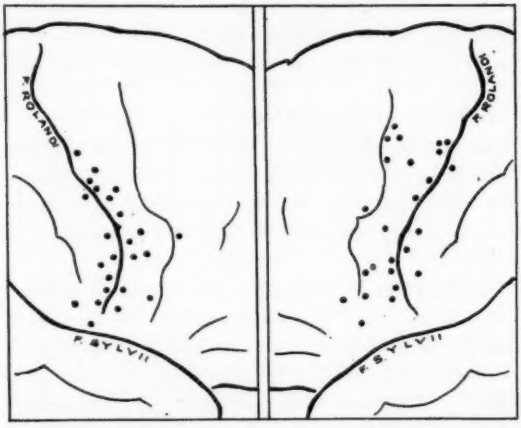

Fig. 1.—Points from which vocalization was produced as a simple motor response in the course of routine electrical exploration of the human cortex are indicated by round dots. The right hemisphere is shown on the left and the left on the right.

The area for vocalization, as a response, occurs below the hand area and above that for swallowing but seems to have no fixed relation in the sequence of the various elements of the face area. In one-half the cases vocalization occurred in association with some additional movement of the lips. In one fourth of the cases it occurred with other motor or sensory accompaniment within the face area. In the final one-fourth it occurred as a solitary phenomenon, without other sensory or motor response. Such observations must be interpreted in accordance with the conditions of observation, for it is relatively easy to see an associated lip movement, but the tongue cannot be seen and may have been moved without our knowledge.

The relation of vocalization to movement of the lips, jaw and tongue is illustrated in figure 2. It may be pointed out that when localization of lip movements was determined as well as that of vocalization, the former was below and the latter above in 9 cases, whereas in 18 cases the relation was reversed. When localization of tongue movements was determined independently, the zone of vocalization was found to be below it in 11 cases and above it in 10 cases.

From these observations, it is obvious that vocalization may occur as an isolated phenomenon, and in that case it might be expected that it would have its own sequential position as compared with movement of the lips and tongue. Actually, its area seems to overlap that for the lips and tongue. Word articulation depends on the coopera-

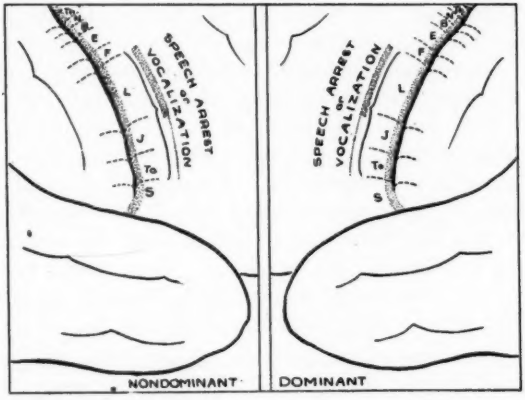

Fig. 2.—Vocalization and speech arrest have a similar localization on the sensorimotor convolutions. Both have most frequently recorded association with lip movements. Sequence of movements, as determined in previous studies, is indicated by letters on the precentral gyrus as follows: *Th*, thumb; *N*, neck; *B*, brow; *E*, eyes; *F*, face; *L*, lips; *J*, jaw; *To*, tongue; *S*, swallowing.

tive movements of lips, tongue and vocalization, so that this close association is not surprising.

ARREST OF SPEECH

Arrest of speech, or the spontaneous statement on the part of the subject that he wanted to talk but could not, was produced by stimulation in much the same sensorimotor area as was vocalization, i. e., in the area corresponding to that of the tongue, the jaw and, especially, the lips (fig. 2), but also occasionally extending down into the area for the throat and swallowing. However, in the dominant hemisphere, speech could also be arrested from other areas, as will be explained presently.

Sensorimotor Cortex.—Arrest of speech was produced by stimulation [2] of the precentral and postcentral gyri at various points in the face area. It was produced equally easily in the dominant and in the nondominant hemisphere and was obtained four times as frequently from the precentral as from the postcentral gyrus. The arrest or slowing of speech seemed to be an isolated phenomenon in two thirds of the cases. In one-fifth there was associated involuntary movement of the lips. Occasionally, sensation in the tongue, mouth or nose, swallowing or movement of the eye or brow was an associated phenomenon. It is, of course, impossible for the observer under the "drapes" to see within the mouth, and some associated phenomena are doubtless missed.

If the stimulation produces movement of muscles of articulation (which have a representation in both hemispheres), and if the patient is making a voluntary effort to use those muscles for the purposes of articulation, there must result a struggle for control between involuntary innervation and voluntary innervation of the same muscles. This usually resulted in control by the electric stimulus, which was variously expressed: "My tongue was paralyzed"; "I lost control of my lips"; "I was unable to control my vocal cords." There is evidence that greater voluntary effort might result in triumph of the voluntary element of innervation. In such a case, a patient said, "I had difficulty in making my lips say 'yes.'" The speech was then slow and labored, and the patient called it "difficult" or "strained." When speech became thick, unintelligible or diminished in volume, it may be that only a small portion of the articulatory mechanism was affected by the electric stimulus.

Speech interference results from stimulation within the sensorimotor convolutions of the two hemispheres with equal frequency. Stuttering was produced once by stimulation of the right postcentral gyrus, and once, in the same patient, slight stuttering was produced by stimulation of the right precentral area.

The localization of points from which speech was arrested is over a considerable extent of the sensorimotor strip. This is due in part to the variability in the comparative extent and position of somatic representations in the human cortex, a variability which is considerably increased by the fact that atrophic focal lesions cause migration of the more normal portions of the cortex toward the site of the lesion.

Of 74 stimulations in the sensorimotor strip, the position of the speech-arresting stimulus was indicated by associated movement of the lips in 14 cases, with other movement or sensation in the face in 9 cases and with hand movement in 1 case. Fifty of 74 stimulations produced

2. A stimulating electrical current which does not produce a positive response may have an inhibitory or paralytic effect on the motor functions represented within reach of the current.

arrest of speech and nothing more. The localization of speech arrest as judged by neighboring stimulation was as follows: just below or above the tongue area or in the tongue area, 12 cases; below the lip area, 20 cases; in the lip area, 4 cases; above the lip area, 11 cases; above the face area and below the throat area, none.

In general, the order of motor and sensory representation in man does not vary. But arrest of speech, like vocalization, seems to have no fixed position within this sequence except that it lies within the zone devoted to the lips, tongue and mouth. This is illustrated in figure 2.

Inferior Frontal Zone—Speech Arrest (Extrarolandic).—In the dominant hemisphere, stimulation of one or two convolutions immediately anterior to the precentral gyrus and just above the fissure of Sylvius may interrupt or prevent speech. If the subject was counting at the time of stimulation, he sometimes slowed down before stopping. This suggests that the patient already had "in mind" the number to be spoken. In such cases, if the stimulation was repeated before he began to count, he was unable to begin at all.

The explanations offered in regard to the inability to speak during such stimulation are interesting: "Didn't know what I was counting"; "could not think." It must be admitted that in some cases stimulation of this area did not stop counting or affect speech, but it is also true that parts of the sensorimotor cortex sometimes do not respond to the strengths of current we care to use.

Parietal Zone—Speech Arrest (Extrarolandic).—Posterior to the sensory representation of the lips and the mouth, stimulation may arrest or interfere with speech. The strength of the stimulating current used here must be higher than the minimum required for response from the sensorimotor area. Stimulation here made it difficult for 1 patient to count backward, although he could still count forward. It caused patients occasionally to use wrong words in naming objects, although they could still speak and could recognize the errors in their speech when they made them.

COMMENT

It is clear that electrical stimulation of the human cortex cannot activate so complicated a process as speaking, any more than it can produce such complicated movements as those of piano playing. Stimulation within the portion of the rolandic cortex devoted to the mouth and lips may arrest speech, or it may produce vocalization. The mechanism of vocalization is a more complex act than the crude movements of extremities that result from cortical stimulation, for it includes coordination of respiratory, laryngeal and pharyngeal muscles. But

vocalization is no nearer an approach to speaking than is the clenching of a fist to the running finger movements of the pianist.

To vocalization must be added numerous other elements before the sound becomes a word, elements which include labial and lingual articulation and certain mental processes. Consequently, it is not surprising that speech may be arrested by an inactivating stimulation in more than one area of cerebral cortex. Without making any claim as to the existence or absence of other areas, e. g., in the temporal lobe, that may be closely related to speaking, we report here three zones for speech arrest that seem to be separable from each other.

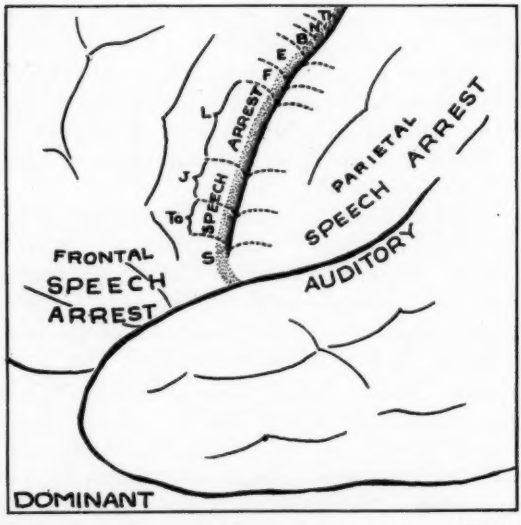

Fig. 3.—Three areas from which arrest of speech was produced by stimulation in the course of routine cortical explorations. *Th, N, B,* etc., have the same representation as in figure 2.

Rolandic Zone—(Sensorimotor) Speech Arrest.—This zone includes the same area in each hemisphere (fig. 2). Speech is arrested by rendering vocalization or articulation impossible. Thus, it is produced by stimulation in the zone of vocalization, which is the same as that of movements of the tongue and lips.

Extraolandic Frontal Zone—Speech Arrest.—This frontal zone of speech arrest in the dominant hemisphere (fig. 3) is situated in one or two convolutions which constitute the frontal operculum, immediately anterior to the lower precentral gyrus. This area is identified with the name of Broca.

The arrest seems to be due to interference with certain processes of thought which are necessary antecedents to speaking. Thus, counting may be caused to slow down after the beginning of stimulation and then stop. The few numbers that the subject was about to utter are pronounced normally before he stops, and he may afterward explain his silence by saying he could not think.

Extrarolandic Parietal Zone—Speech Arrest.—This zone, as indicated in figure 3, is found in the parietal cortex of the dominant hemisphere anterior to the fissure of Sylvius and posterior to the postcentral gyrus. Like the frontal zone of arrest, stimulation here does not seem to paralyze any motor mechanism. It may interfere with correct choice of words when it does not prevent counting.

CONCLUSION

There is a zone in the sensorimotor convolutions of each hemisphere in which vocalization, lip movement and tongue movement are represented bilaterally (fig. 2). These areas may be called the word articulation zones. If one zone is removed, the functional activity of the other makes speech possible, although there may be transient anarthria.

Without discussion of the temporal lobe, and without referring to clinical opinions of aphasia, it may be pointed out that our evidence indicates the presence of a frontal speech area and a parietal speech area in the dominant hemisphere (fig. 3). The functional integrity of these two areas is essential to the mental processes involved in speaking.

These two speech areas might be considered a second motor and a second sensory area corresponding to the sensorimotor zone for the lips, tongue and vocalization. But the essential neuronal connections between these second speech areas and the sensorimotor zone are not transcortical, as shown by the fact that the face area, as well as the dominant arm area, can be removed without producing aphasia.[3]

Consequently, the essential neuronal connections of the second speech areas must be via subcortical pathways to the sensorimotor word articulation area of the rolandic convolution on both sides.

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3. The precentral gyrus in which the dominant hand is represented can also be excised without postoperative aphasia.

POLIODYSTROPHIA CEREBRI PROGRESSIVA (INFANTILIS)

Report of a Case

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DURING the last thirty years, cases of hereditary disease have occurred in which the white matter of the brain was extensively destroyed and the cerebral cortex and the gray matter were on the whole preserved. Originally, this condition was called diffuse sclerosis of the brain. The name is inappropriate, for two reasons: First, it is more natural to name a disease after its initial stage than after its cicatrizing, terminal, stage. Second, the name diffuse sclerosis of the brain is not explicit, for it has been used to designate very different conditions: Schilder's disease,[1] which is probably a chronic virus infection; extensive syphilitic sclerosis of the brain; certain forms of glioblastoma, and, finally, three types of hereditary diseases: the acute early infantile type,[2] the subchronic infantile type of Scholz [3] and the chronic juvenile type of Pelizaeus and Merzbacher.[4] Bielschowsky [5] proposed the designation leukodystrophia cerebri progressiva hereditaria for these hereditary abiotrophies. The name is somewhat ponderous, but it is clear and comprehensive; we propose to maintain it.

There exists a fairly extensive literature on leukodystrophia cerebri progressiva. But not until twenty years ago was attention drawn to cases of a condition which is in direct contrast to leukodystrophy: a condition in which the gray matter of the brain is more or less exten-

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1. Schilder, P.: Zur Kenntnis den sogenannten diffusen Sklerose, Ztschr. f. d. ges. Neurol. u. Psychiat. **10**:1, 1912; Die Encephalitis periaxialis diffusa (nebst Bemerkungen über die Apraxie des Lidschlusses), Arch. f. Psychiat. **71**:327, 1924.

2. Krabbe, K. H.: A New Familial Infantile Form of Diffuse Brain Sclerosis, Brain **39**:74, 1916.

3. Scholz, W.: Klinische, pathologisch-anatomische und erbbiologische Untersuchungen bei familiären, diffusen Hirnsklerose im Kindesalter, Ztschr. f. d. ges. Neurol. u. Psychiat. **99**:651, 1925.

4. Merzbacher, L.: Ueber die Pelizaeus-Merzbachersche Krankheit, Zentralbl. f. d. ges. Neurol. u. Psychiat. **32**:36, 1923.

5. Bielschowsky, M., and Henneberg, R.: Ueber familiäre diffuse Sklerose, J. f. Psychol. u. Neurol. **38**:12, 1927.

sively wasted, while the white matter is preserved. We have found only 3, perhaps 4, cases of this type reported in the literature: Freedom's[6] in 1927 and 1931; Alpers',[7] in 1931; Ford's,[8] in 1937 and 1944, and Somoza's, cited by Alpers,[7] which was to have been published in 1931, but which we have not been able to find in the *Quarterly Cumulative Index Medicus* or elsewhere. These cases will be mentioned later. We have had the opportunity to study a case clinically and anatomicopathologically; as cases of this disease are rare, we shall report it in some detail.

REPORT OF CASE

History.—H. D. B. born on April 29, 1944, the son of a painter. The parents were cousins; a pair of great-grandparents and a pair of great-great-grandparents were likewise cousins. No cases of organic nervous disease, cramp or mental debility had occurred in the family. The patient had a sister, four years older than he. She, their mother and her 4 siblings presented the same dental anomaly as the patient; that is, the milk teeth at an early age became brown and fragile and cracked. The mother's permanent teeth and those of her brothers and sisters were good. The mother's health had been good during her pregnancy except for nausea in the first months.

The child was born by normal delivery. His weight at birth was 3,600 Gm. and his length 53 cm. He was breast fed in a normal manner until the age of 6 months. After that he had ordinary infant food, with cod liver oil preparations, hip juice and malt extract. He moved in a natural manner.

Mental and motor development seemed normal during the first seven or eight months of life; then it was somewhat slower. The child could not sit upright until the age of 1 year; he could stand alone when he was 18 months of age and could walk a few steps with support, but he was slow in moving his legs. The mother thought that he was somewhat dull; he seemed to recognize his parents, but he never smiled at them. However, he smiled at his sister when she played with him. He occupied himself with his playthings, but he was not able to eat a sandwich that was put in his hand, although his appetite was good. During the day he was quiet, but at night he was often sleepless and fretful. At the age of 1 year he could say *"mammam"*[9] and *"bang."*

The first tooth appeared when he was 6 months old, but one-half year later the teeth began to darken and to break. The bowels moved slowly; the other functions were normal.

At the age of 18 months, in November 1945, he was admitted to the children's department of Sundby Hospital, Copenhagen. The chief physician, Dr. Carl Friderichsen, gave us permission to use the history. Physical examination presented nothing abnormal referable to the nervous system. The skull was firm; the anterior

6. Freedom, L.: Ueber einen eigenartigen Krankheitsfall des jugendlichen Alters unter dem Symptomenbilde einer Littleschen Starre mit Athetose und Idiotie, Zentralbl. f. d. ges. Neurol. u. Psychiat. **46**:196, 1927; Cerebral Birth Palsies, Arch. Neurol. & Psychiat. **26**:524 (Sept.) 1931.

7. Alpers, B. J.: Diffuse Progressive Degeneration of the Gray Matter of the Cerebrum, Arch. Neurol. & Psychiat. **25**:469 (March) 1931.

8. Ford, F. R.: Diseases of the Nervous System in Infancy, Childhood and Adolescence, ed. 2, Springfield, Ill., Charles C Thomas, Publisher, 1945, p. 334.

9. This means in Danish "food," not "mother."

fontanel was closed. Bühler's and Hetse's tests showed a development of 46 per cent. It was difficult to obtain contact with the child. Examination of the heart, lungs and abdomen showed nothing abnormal. The testes had descended.

Four months later he was again admitted to that hospital. Development seemed then to have been completely arrested. He was entirely uninterested in the surroundings; he did not play and looked at the parents only for short moments. He could not masticate and would not bite; it was necessary for the nurse to feed him and to give him half-liquid food. He did not say anything, but he cried a great deal in the night.

This admission was especially because of coprostasis. Roentgenologic examination of the colon revealed the picture of megasigmoid. Roentgenograms of the head presented a normal condition. Physical examination revealed the same condition as on the first admission. Ophthalmologic examination gave normal findings. The child followed a moving candle with the eyes. The pupils were rather large and reacted well to light. The deep reflexes were not exaggerated. The plantar response was not characteristic. The temperature was normal during the two hospitalizations.

After his discharge, the child's condition grew steadily worse. He was now unable to stand or to support himself on his legs; he did not play; he would not eat ordinary food, and he salivated constantly. His mother said she doubted whether he could hear. The bowels had always moved slowly and irregularly, sometimes at intervals of a week. From June 7 until July 25 he was under observation in the Children's Hospital, Martinsvej. The chief physician, Dr. A. Rothe Meyer, permitted the use of the history.

At the time of admission the child could not stand or sit. He was completely without interest in his surroundings; he did not look at anything or respond when spoken to, but he reacted to loud noises; he never smiled, but he salivated constantly. He was able to swallow only liquid food. The tonus of the extremities was normal. The deep reflexes were very active, with an enlarged reflexogenic zone. Muscular power was hardly diminished, but the movements were ataxic and the hands showed gross trembling. During the examination attacks of laughter occurred suddenly.

On ophthalmologic examination, on June 25, the patient did not follow a moving object with the eyes. The size, position and movement of the eyes were not remarkable; the disks and fundi were entirely normal. The hemoglobin concentration and the urine were normal. A roentgenologic examination of the colon at this time resulted in a somewhat more doubtful diagnosis of megasigmoid. After his discharge the condition did not present any remarkable change.

In October and November 1946, the child was again hospitalized in the Children's Hospital, Martinsvej. Physical examination showed a condition similar to that at the last hospitalization. The patient was "jumpy" but otherwise dull and uninterested. Sometimes small contractions of the arms appeared. The anterior teeth on the maxilla looked worn, not simply carious. There was some degree of gingivitis.

On November 6 the child suddenly became pale and cyanotic; he vomited, and the pulse was feeble. After this attack he was somnolent. Small contractions of the face, arms and legs occurred. The temperature increased up to 39.5 C. (103.1 F.) but became normal again in three days, and the condition was unchanged.

On November 8 a spinal puncture was performed. The spinal fluid was limpid and contained 285 erythrocytes and 26 lymphocytes per 3 cu. mm.; no bacteria were noted on direct microscopic examination or in cultures. The protein content was normal.

On November 17 the patient was transferred to the neurologic department of Municipal Hospital (Kommunehospitalet), Copenhagen.

Examination.—The child was entirely unresponsive when addressed. It was necessary to open his mouth and pour the food into it, but he swallowed it in a normal manner, without gulping. He never laughed or smiled. Sometimes he cried, but he made no other sound. He slept most of the day. The head was somewhat small but not exactly microcephalic. The anterior fontanel was closed; a small depression corresponding to its position could be felt. The teeth were worn; only stumps of the incisors remained.

The disks and fundi of the eyes were normal. The pupils were equal; they changed in size and reacted inconstantly to light, possibly owing to changing accommodation. Sometimes he followed a light with the eyes and sometimes not. His eyes were very unquiet, but there was no asynergia or peresis of movements. There was no facial paresis. The expression was not imbecile, but somewhat immobile and rather depressed. He did not react to noises.

The upper extremities were generally flexed at the elbows; the hands were clenched. He moved them a little, through undulating lines, but with small excursions. Sometimes small, sudden myoclonic movements appeared, chiefly extension jerks. All the joints were freely moved, without pain. Tonus was considerably increased and of spastic character. The deep reflexes were very active. He reacted to pinprick by crying and somewhat incomplete parrying.

The median lobe of the thyroid gland was palpable and seemed of normal size and consistency. Stethoscopic examination of the heart gave normal sounds. The liver and spleen were not enlarged. The abdominal reflexes were absent. The spinal column was of normal form and freely movable; but when he was sitting up the back as a whole presented kyphosis. If the body was lifted by a hand placed below the lumbar region, it became normally lordotic. On attempts to raise him, the head fell backward. When he was bent forward, the head fell forward but was kept a little raised by the tensed muscles of the neck.

All the joints of the lower extremities could be freely moved. Sometimes there was a slight increase of tonus with passive movements; at others a sudden spastic resistance occurred. The knee jerks were very active and could be elicited from the upper half of the tibia but not from the lower half. There was no patellar or ankle clonus. The Rossolimo reflex was feeble. The Babinski sign was strongly elicited on both sides. It could be elicited from the sole, but not from the dorsum of the foot or from the leg. He reacted to pinprick on the lower limbs, as well as over the trunk and the upper limbs. The legs lay extended, sometimes crossed. When an attempt was made to have the child stand and support was relaxed, he sank down at the hips and knees. Sometimes he lifted a leg, with flexion movements of the hip or knee. The feet became cyanotic when he was placed upright.

The skin was dry. Nummular, sharply delimited, probably mycotic, plaques were dispersed over the trunk and extremities.

Laboratory Studies.—Lumbar encephalography was performed on Dec. 4, 1946; 30 cc. of cerebrospinal fluid was evacuated and a corresponding amount of air was injected. The spinal fluid contained 147 lymphocytes per 3 cu. mm. The protein content was normal. The Wassermann and Meincke reactions of the spinal fluid and blood serum were negative. The hemoglobin concentration and the urine were normal, and the sedimentation time of the blood was normal. The encephalogram presented considerable dilatation of the left ventricle, which was not displaced. The filling with air was not sufficient, so that the ventricular system of the right side was incompletely visualized.

Course of Illness.—The child seemed to be well after the encephalographic study. After admission, he became quieter and cried less. He seemed to like sweets very much, spitting out all other food; so it was necessary to put sugar in all his food.

He always lay on his back and would not lie on his side. There were continuous myoclonic contractions of the extremities.

Since admission the child had received intramuscular injections of 2 cc. of "benadon" four times a week and 2 cc. of "becozym"[10] twice a week. No other medication was given.

For a long time a certain improvement was apparent. The child was quieter and cried less; his appetite was better; his weight increased, and he seemed able to stand better. The myoclonic movements decreased for some time, but they again increased.

On December 21 rhinitis appeared and was constant; it grew worse and on Jan. 13, 1947 the temperature increased to 40 C. (104 F.). He cried and became restless, and myoclonic movements increased. Respiration became rapid and shallow; the extremities were cyanotic. He received injections of "alfasol" (a preparation of sulfanilamide), without any effect, and died on January 14.

On January 8 an ophthalmoscopic examination had shown that the disks were pale but without signs of edema. His weight on admission had been 10.5 Kg.; eight days before his death it was 13.2 Kg.

The diagnosis of members of the department was Schilder's disease, or leukodystrophia cerebri progressiva hereditaria (Scholz type).

Clinical Summary.—A boy died at the age of 2½ years, with symptoms of a progressive disease of the brain. There was no disposition to any similar disease in his family, but his parents, as well as a pair of great-grandparents and a pair of great-great-grandparents, were cousins. The patient's sister, his mother and her 4 sisters and brothers had a dental anomaly, similar to that in the patient. The child seemed fairly normal until the age of 7 or 8 months, when development became somewhat retarded; and at the age of 15 or 16 months retrogression set in. This retrogression perhaps became stationary during the last six months of his life. The fully developed clinical picture (at the age of 2 to 2½ years) was as follows: complete lack of interest in the surroundings; an apparent absolute defect of mental content; possible feebleness of vision, owing to incipient optic nerve atrophy; aphasia and dysphagia; spasticity of all four extremities, with active deep reflexes and a Babinski sign; pareses and some ataxia of all the extremities, with preservation of the trophic condition of the muscles and of sensibility; pareses of the muscles of the trunk; myoclonic contractions of the extremities, but no epileptiform fits at any time, and, further, a curious crumbling of the teeth (probably a familial sign). Encephalograms showed dilatation of the ventricular system on the left side, and possibly also on the right. The spinal fluid on two examinations presented pleocytosis but no increased protein.

Autopsy.—One-half hour post mortem a suboccipital-subarachnoid injection of 40 cc. of formaldehyde solution U.S.P. in saline solution (1:4) was given. The weight of the body was 13 Kg.; the length, 90 cm.

Postmortem examination twenty-two hours later revealed atelectasis and edema of the lower parts of the lungs. On section, the surface of the liver presented gray-yellow spots on a darker reddish brown ground. The colon was not dilated, and the organs presented a healthy appearance. Specimens from the thymus, thyroid, lungs, spleen, kidneys, liver and testes were taken for histologic examinations.

Microscopic study showed atelectasis and edema of the lungs, acute stasis and slight postmortem change of the liver, slight stasis of the spleen and an otherwise normal condition.

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10. One cubic centimeter of "becozym" contains 1 mg. of thiamine hydrochloride, 2 mg. of riboflavin, 20 mg. of nicotinamide, 2 mg. of adermin and 3 mg. of pantothenic acid.

The brain was preserved in formaldehyde solution U.S.P. in saline solution (1:4) for a fortnight. It was somewhat atrophic, especially the frontal lobes, where the basal gyri were narrow lists between the broad, deep sulci (fig. 1), whereas there was pachygyria of the superior frontal, precentral and postcentral gyri. The pons, medulla and cerebellum were normal in form and size. By mistake, the spinal cord was not removed for examination.

The brain tissue had a dense consistency, partly because of the intracranial injection of the saline–formaldehyde solution U. S. P. fixative, but also perhaps because of alterations in the brain. The pia and the arachnoid were thickened and lay like a white, folded veil over the atrophic brain. Frontal section of the brain revealed a strange picture. The cortical gray matter was shrunken, being 1 to 3 mm. in thickness, and soft and spongy in the deeper parts, whereas the white matter

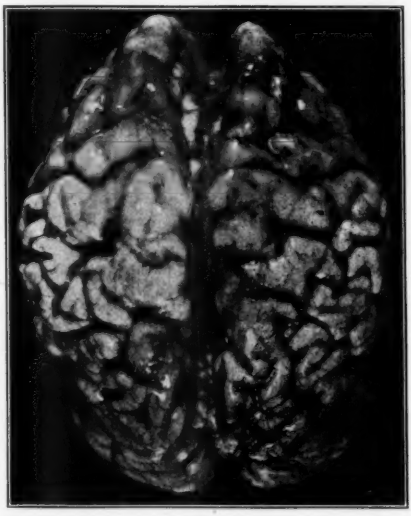

Fig. 1.—Brain seen from above, showing cortical atrophy, especially in the frontal lobes, and pachygyria in the motor regions.

and the basal ganglia appeared normal except in some of the gyri, where the tissue was grayish and the cut surface gritty (fig. 2). The ventricles were somewhat dilated, especially the third, which measured 1 cm. in diameter. For histologic purposes, specimens were taken from the cortical gray matter in the frontal, temporal and parietal lobes and from the island of Reil and the basal ganglia. Specimens were also taken from the cerebellum, the medulla oblongata and the pons.

The pia and the arachnoid were thickened with fibrous tissue; they were more cellular than normal, with large mononuclear cells having a central or slightly eccentric, round nucleus, plasma cells and lymphocytes. In several places the pia and arachnoid were undifferentiated and made up of fetal connective tissue.

The atrophic cortical gray matter also presented a characteristic histologic picture. The alterations were nearly the same throughout the gray matter but were graduated in severity. The stratification of the neurons was nearly absent except

in the insula (figs. 3 and 4). The loss of neurons was compensated by proliferation of fibrillar and protoplasmic astrocytes. Chiefly superficial, undifferentiated nerve cells were observed; in the deeper layers there were also polygonal and triangular nerve cells, with the long axis parallel with or perpendicular to the surface (fig. 5). The Nissl substance was lacking, and many of the nuclei were placed eccentrically.

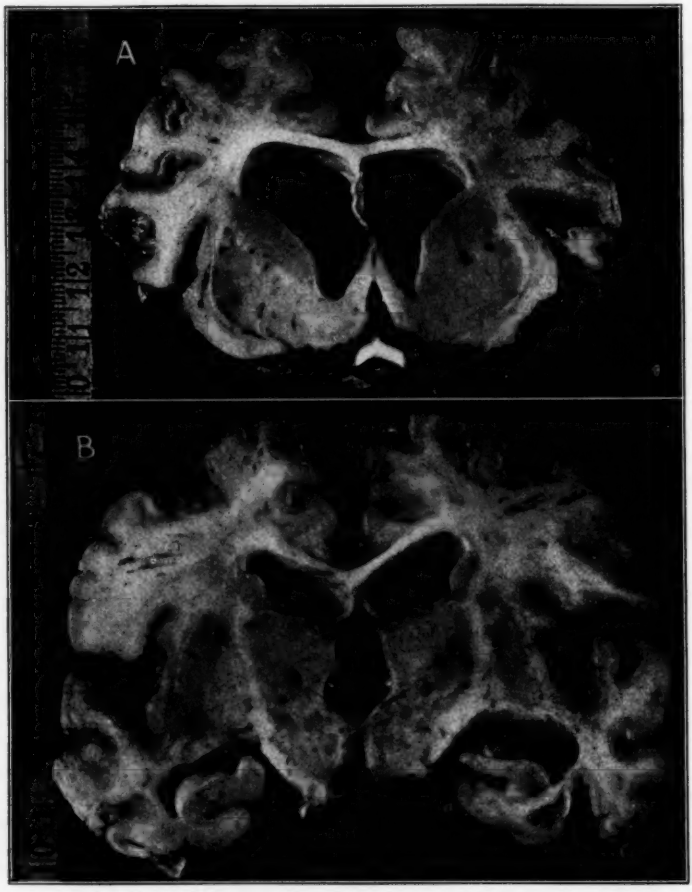

Fig. 2.—*A*, section through the frontal lobes and caudate nuclei showing the cortical atrophy, the dilated ventricles and the normal basal ganglia. *B*, section through the parietotemporal region and thalamus, showing pronounced cortical atrophy, normal white matter, normal basal ganglia and slightly dilated ventricles.

In the deeper layers there appeared occasional traces of stratification; most of the cells in the third and fourth cortical layers were astrocytes, which were represented by a spongy reticulum (fig. 6). In the deeper layers were a few nerve fibers. In

the parts of the cortical gray matter where the tissue was soft was a moderate proliferation of microglia cells, containing lipid granules; these cells were especially arranged around the vessels. In the most atrophic gyri the tissue was almost entirely composed of spongy glia, with a few typical neurons.

In the occipital lobes occurred a heavy subpial proliferation of glia cells—piloid astrocytes—concentrically arranged and forming round balls of fibrils (fig. 7*A*). The only part of the cortical gray matter where the histologic picture was normal was the cornu ammonis, which contained normal pyramidal neurons (fig. 7*B*). The vessels showed no alterations.

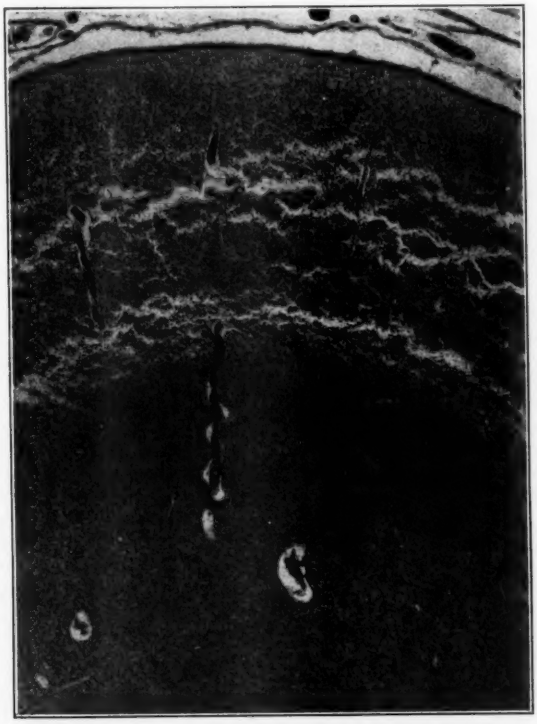

Fig. 3.—Cerebral cortex of the parietal lobe with disorganization of the stratification and proliferation of spongy glial cells. Magnification × 60; hematoxylin-eosin stain.

The basal ganglia and the white matter seemed normal; here and there were a few microglia cells containing lipid granules. The myelin sheaths were normal.

The ependyma and the walls of the ventricles were normal except at the base of the third ventricle. Here were small polyps covered with ependyma, and in other places the ependyma was replaced by astrocytes, macrophages containing blood pigment, and lymphocytes. As seen from the foregoing description, the most important pathologic features of the brain were dysplasia and partial atrophy of the

cerebral cortex, with a secondary increase in the neuroglia, whereas the white matter was fairly well preserved. The same picture occurred in the basal ganglia, the cerebellum and the brain stem.

CLINICAL AND ANATOMICOPATHOLOGIC COMPARISON OF CASES

Clinical Comparison.—Freedom's case was that of a girl who died at the age of 19. There was no familial disposition. Birth was normal. The child was dull and was not able to sit up before the age of 3

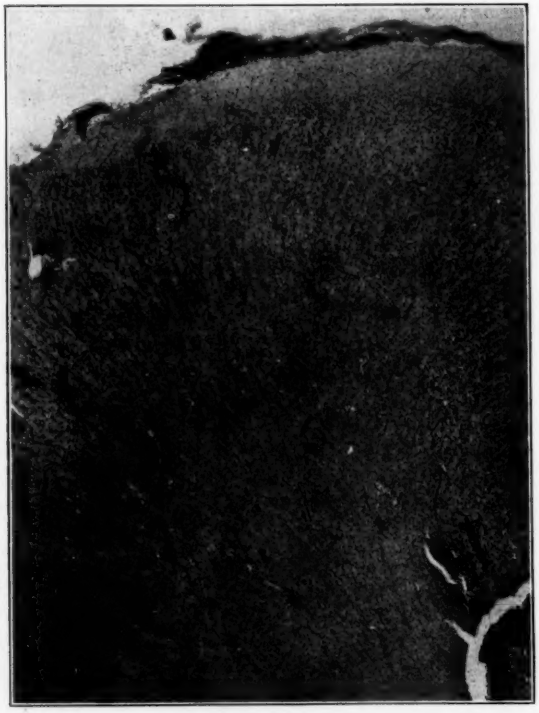

Fig. 4.—Cerebral cortex from the parietal lobe of a physically normal child of the same age as that of the patient whose brain is shown in *A*. Magnification × 60; hematoxylin-eosin stain.

years. At this time she said words that sounded like "papa" and "mama." At the beginning of the fifth year she attempted to walk, but her gait was unsteady and she frequently fell. At the age of 5 years epileptiform seizures commenced; at the same time she showed a tendency to contracture of the lower limbs. From 9 to 10 years of age she presented involuntary twitchings of the muscles of the face,

fingers and extremities. During the following years she could perform only the simplest personal duties. At the age of 19 she was completely demented. There was no spontaneous speech; when questioned, she mumbled only an indistinct reply. She was unable to walk or to sit up in bed. She was incontinent of bowel and bladder. The fundi were normal, and there were no symptoms referable to the cranial nerves. The upper extremities were rigid but not atrophic or

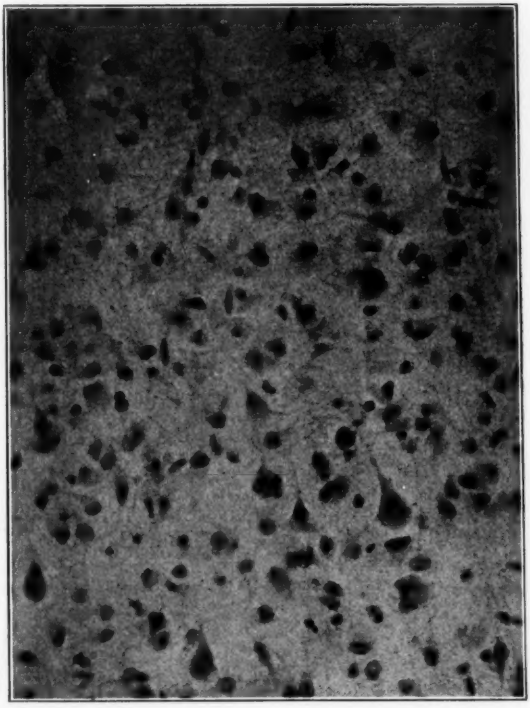

Fig. 5.—Polygonal and triangular neurons form the third and fourth layers of the cortex, showing lack of Nissl substance and eccentrically placed nuclei. The long axis of the cells takes various directions. The glial cells have proliferated. Einarson's gallocyanine stain; magnification × 305.

paralytic. The lower extremities showed flexion contracture; the deep reflexes were hyperactive; patellar and ankle clonus and an extensor response were present on both sides. She often had epileptic seizures.

Alpers, in addition to Freedom's case, cited a case of Somoza's, that of a girl aged 8 months who had asphyxia at birth. She presented severe hyperkinesia, opisthotonos and choreiform movements. No

further clinical description was given. Alpers' case was that of a girl who died at the age of 3 months. Birth had been normal and she developed normally during the first weeks of life. Then she began to have attacks of generalized stiffness. She could crawl but was unable to hold up her head. She slept a great deal. The patellar reflexes were active; the Babinski sign was not elicited; abdominal reflexes

Fig. 6.—Degeneration of the cerebral cortex with proliferation of spongy glial tissue, especially in the third and fourth layers of the cortex. Magnification × 100; Heidenhain's stain.

were absent. The pupils did not react to light; the optic nerves were pale; she seemed to be blind. Motor restlessness and attacks of universal rigidity developed. The rigidity grew increasingly severe. Several days before death she collapsed, whereupon the convulsive attacks ceased.

Ford described the case of a girl who began to have convulsive seizures, at first associated with fever, at the age of 6 months; later

the fever ceased, but the seizures continued. The convulsions became more frequent and severer. Many were confined to the left side. Before the end of the first year the child was deteriorating. She seemed to be blind and did not respond to auditory stimuli. She could no longer hold up her head or sit up without support. There were occasional vomiting and some loss of weight. At the age of 14 months examination showed fairly good physical development but no evidence of any

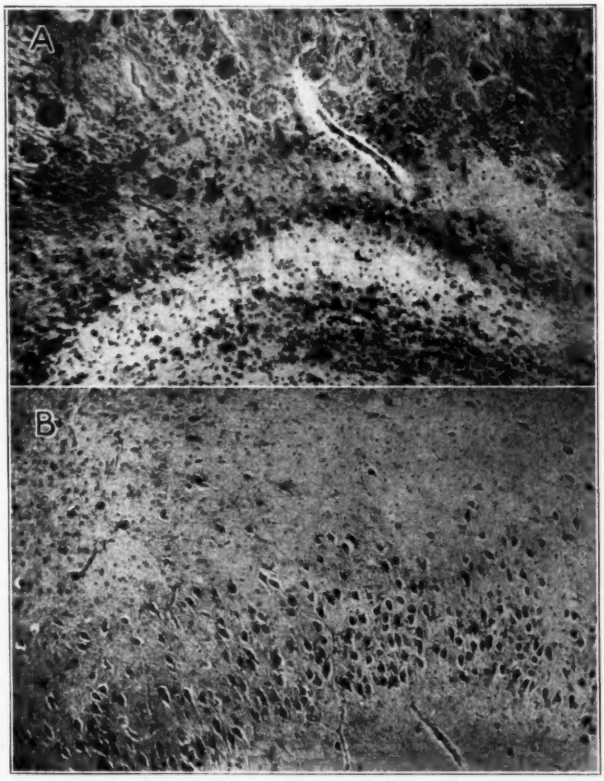

Fig. 7.—*A*, section of the occipital lobe, showing subpial proliferation of glial tissue, with formation of round balls of fibrils, and degeneration of neurons. Magnification × 70; hematoxylin-eosin stain. *B*, hippocampus with normal stratification. Magnification × 70; hematoxylin-eosin stain.

mental growth. She seemed deaf and blind and made no attempt to speak. The optic fundi were normal; the pupils reacted to light. There was general muscular rigidity; the deep reflexes were increased. Ankle clonus was abolished; plantar reflexes were normal. No involun-

tary movements were present. The spinal fluid was normal. Ventriculograms revealed that the right lateral ventricle was somewhat dilated. The course was progressively downhill. The child died in a series of violent seizures, at the age of 16 months.

Comparison of the aforementioned 3 cases (Somoza's can scarcely be considered) with our case reveals that all presented symptoms referable to the central nervous system. In all 4 cases the extremities were hypertonic, with increased deep reflexes. Otherwise, the course and the symptoms showed considerable differences. Freedom's patient seems to have been defective from birth. Alpers' patient was apparently normal during the first weeks of life. Ford's patient presented the first pathologic signs when she was 6 months old. Our patient did not show any definite arrest of development until the age of 8 months. The children died at the ages of 19 years, 3 months, 16 months and 2½ years, respectively. Freedom's and Ford's patients had general epileptiform seizures. Alpers' patient presented attacks of generalized rigidity. Our patient had myoclonic seizures but no epileptiform fits. Alpers' and Ford's patients were blind; Freedom's patient and ours probably were not. Our patient had a possible incipient atrophy of the optic nerve. In the other 3 patients the fundi of the eyes seemed normal. In Freedom's and in our case a Babinski sign was elicited; in Alpers' and Ford's cases the plantar responses were normal. It is difficult to evaluate the mental qualities in Alpers' patient, who died at the age of 3 months. In the other 3 patients some degree of mental debility had developed.

Although the picture presents considerable variations, the fundamental features may be summed up as follows: The patients are children who in the first year of life present progressive deterioration of the mental faculties combined with progressive spastic pareses of all the extremities. To this may be added epileptiform fits, myoclonic seizures, blindness and deafness, but not appearing in a constant manner. The fact that so few and such variable cases have been published renders an exact diagnosis difficult. In the neurologic department of the Municipal Hospital, we had made the diagnosis of leukodystrophia cerebri progressiva, Scholz type. It is curious, perhaps, that we should have made a diagnosis quite the opposite of that revealed at autopsy: The condition was not a degeneration of the white matter with preservation of the gray matter, but a degeneration of the gray matter with preservation of the white matter. As a matter of fact, deficiency of neurons may give the same symptoms whether the nerve cells or the nerve fibers are primarily affected.

If experience with this rare disease increases in the future, the chances of making a correct diagnosis in such cases will be better. Temporarily, one must exclude syphilis, intercranial tumors and such

characteristic forms of mental debility as mongolism, tuberous cerebral sclerosis and familial amaurotic idiocy. In the cases we have described here, we can state only that the disease is a progressive cerebral disorder, abiotrophic or inflammatory, which attacks the regions of the cerebral hemispheres concerned with mental and motor functions.

Anatomicopathologic Study.—Common to all 4 cases is the presence of a disease of the brain involving predominantly the gray matter; i. e., the nerve cells in the first line were destroyed, while the myelinated nerve fibers were not primarily affected.

In addition to this fundamental common feature, the anatomicopathologic picture presented rather considerable variations in the character, course and distribution of the morbid processes. In our case, there seemed to be two processes. First, the cellular layers of the cortex were disorganized. This disorganization was probably congenital, of fetal origin; it cannot be excluded, but it seems less probable that it was a consequence of a later degeneration of the nerve cells. Second, there appeared a series of features which indicated a postnatal progressive process: a destruction of nerve cells in the cortex of the brain and a secondary compensation of the defects by fibrillary neuroglia cells, especially by astrocytes. In addition to these positive features, certain negative ones must be emphasized. Nothing indicated that the disease was due to an active inflammatory process or its results. The strikingly uniform systematic distribution of the processes and the limitation to the cortex of the brain, with sparing of the neighboring areas, indicates with great probability that the process was an abiotrophic, not an inflammatory one. Further, the absence of active inflammatory features and the very limited degree to which scavenger cells with products of protein or lipid destruction were seen indicate that the process of destruction which must be supposed to have taken place was finished.

In Freedom's case, as in ours, pronounced changes in the gray matter of the brain were observed. However, they were not, as in our case, confined to the cortex of the hemispheres. The striatum presented severe alterations; the pallidum still more extensive changes, and the hypothalamus, most extensive of all. In the cortex, the process was most prominent in the island of Reil, which in our case presented only slight alterations. As for the rest of the cortex, the changes were most pronounced in the occipital portion and least in the frontal part, whereas in our case they were rather uniform throughout the whole cortex. In Freedom's case the disorganization of the cytoarchitecture was not so pronounced as in ours. On the other hand, the acute modifications were far more intense. The stains for fat showed a great destruction of lipids, the picture suggesting dementia paralytica. In some areas almost the entire cortex was destroyed.

In Alpers' case (the infant was only 3 months old at death) the cytoarchitecture was much better preserved, and in only a few places were the alterations so pronounced that it was effaced. The changes in the gray matter, as in Freedom's case (in contrast to ours), extended to the basal ganglia. The pathologic involvement of the nerve cells was altogether much severer than in our case. The process showed a similar distribution, presenting, particularly in the deeper layers, a decided status spongiosus. Corresponding to the absence of ganglion cells, the neuroglia cells were considerably increased, especially the astrocytes. Alpers noted a large number of ganglion cells in the white matter. If this observation is correct, it is a curious phenomenon. In the white matter in our case were observed a great number of neuroglia cells, rich in protoplasm, presenting the appearance of scattered ganglion cells. One must consider the possibility that the cells in the white substance which Alpers called ganglion cells may have been such protoplasmic glia cells. Furthermore, in some areas in Alpers' case the brain showed an enormous vascularization, with dilated capillaries, almost resembling an angiomatous formation. We observed no such vascularization in our case. Alpers also noted in the white substance a large tract of giant cells with three to eight nuclei and an enormous amount of protoplasm. We did not observe a similar phenomenon in our case. But we must admit that in the case of early infantile cerebral sclerosis (leukodystrophia cerebri hereditaria) which one of us (K. H. K.) described in 1916,[2] such giant neuroglia cells were present in the brain.

Ford's case differed somewhat from the others. The atrophy of the brain was predominantly unilateral. In the atrophic hemisphere the neurons were extensively destroyed in the cortex, especially in the third and fourth laminas, which, as in Alpers' and in our case, presented a status spongiosus. The microglia (with lipid granules) exhibited moderate proliferation, but there were no signs of inflammation. As in our case, the white matter and the basal ganglia were relatively undamaged. It was a peculiar feature that the cortex of the cerebellum presented severe destruction of the ganglion cells. The Purkinje cells had largely disappeared; the cells in the stratum moleculare, almost entirely.

PATHOLOGIC CLASSIFICATION

The final question is how to place this disease in the pathology of the nervous system. First, it may be established with great certainty that the disease is not an inflammatory process or a sequel of an inflammation. It is characteristic that hardly anywhere is there infiltration of the walls of vessels, nor are there scavenger cells or plasma cells. This indicates that the process in the nervous system is probably complete, that there is no further destruction of the cerebral tissue. However, there remains the question whether the anomaly is a congenital defect or

whether it is a progressive abiotrophy. Both possibilities must be considered. The complete disorganization of the cytoarchitecture of the cerebral cortex, together with the presence of many neuroblasts, as well as other phenomena, indicate a retarded development in fetal life, perhaps somewhat like that occurring in tuberous sclerosis of the brain. There is no doubt that later a progressive destruction of nerve tissue, with replacement by fibrillar neuroglia tissue, takes place. On this point the clinical and the anatomopathologic findings agree. The history in our case indicates that the child was fairly normal through the first months of his life, although his development was possibly somewhat retarded. However, the clinical picture gives the impression that there was a decrease in the mental function comparable to that in the function of the pyramidal tracts.

Both the congenital disorganization and the progressive abiotrophy are closely connected with the gray substance of the brain. In the 3 other cases described in the literature the degenerative processes were observed in the cortex, the basal ganglia and the cerebellum. In our case it was limited to the cerebral cortex, but was fairly equally distributed throughout the cortex of both hemispheres.

The disease forms a strange contrast to leukodystrophia cerebri progressiva. In the latter, the entire white matter of the corona radiata is destroyed, but the cortex is well preserved. In the present case, as in the cases reported by Freedom, Alpers and Ford, the white matter was relatively well preserved, whereas the gray matter was both disorganized and destroyed. None of the three authors who first described this disease has given a name to the disease; they have only characterized it as "progressive degeneration of the gray matter of the brain." It would be practical to have a name (Greek and Latin) for the disease, and we propose that it be designated—in contrast to leukodystrophia cerebri progressiva—as poliodystrophia cerebri progressiva (infantilis).

Dronningens Tvaergade 6 (Dr. Krabbe).

EFFECT OF CARBON DIOXIDE ON ACROCYANOSIS IN SCHIZOPHRENIA

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THE OCCURRENCE of cool blue hands in many patients with schizophrenia is well recognized. According to Olkon,[1] cutaneous capillary microscopy over the finger nail fold during life in such instances reveals a decrease in the number of visible capillaries. The capillaries appear pale, bizarrely formed and, in places, irregularly dilated; blood flow through them is irregular and slow. However, the previous work of Schrijver-Hertzberger[2] and the large number of earlier studies discussed in Suckow's[3] exhaustive review strongly suggest that changes such as these are not constantly found in patients with schizophrenia and are not specific to that disease. A number of authors[4] have also found evidence of stasis in blood drawn from the antecubital vein of schizophrenic patients, and Abramson and

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1. Olkon, D. M.: Capillary Structure in Patients with Schizophrenia, Arch. Neurol. & Psychiat. **42**:652 (Oct.) 1939.

2. Schrijver-Hertzberger, S.: Ueber das Capillarbild bei Psychosen, Ztschr. f. d. ges. Neurol. u. Psych. **141**:261, 1932.

3. Suckow, H.: Capillarmikroskopie und Psychiatrie. Kritisches Referat, Zentralbl. f. d. ges. Neurol. u. Psychiat. **64**:417, 1932.

4. (*a*) Segal, L., and Hinsie, L. E.: The Cyanosis of Dementia Praecox: A Study of Gas Relationships in the Blood, Am. J. M. Sc. **171**:727, 1926. (*b*) Notkin, J.; Greeff, J. G. W.; Pike, F. H., and Killian, J. A.: Changes in the Clinical Signs and Laboratory Findings in Various Types of Psychosis Under the Influence of Subcutaneous Administration of Oxygen, Am. J. Psychiat. **89**:1271, 1933. (*c*) Looney, J. M., and Childs, H. M.: The Lactic Acid and Glutathione Content of the Blood of Schizophrenic Patients, J. Clin. Investigation **13**:963, 1934. (*d*) Steinfeld, J., and Gerber, L.: Oxygen Content of the Blood During the New Treatments for Schizophrenia, Illinois M. J. **72**:351, 1937. (*e*) Thompson, J. W.; Corwin, W., and Aste-Salazar, J. H.: Physiological Patterns and Mental Disturbances, Nature **140**:1062, 1937. (*f*) Looney, J. M., and Freeman, H.: Oxygen and Carbon Dioxide Contents of Arterial and Venous Blood of Schizophrenic Patients, Arch. Neurol. & Psychiat. **39**:276 (Feb.) 1938.

associates [5] concluded from plethysmographic measurements that the peripheral blood flow is often low in the hands but not in other parts of the extremities of patients with schizophrenia. In addition, Jung and Carmichael [6] found evidence of vasoconstriction in the hands of patients in catatonic stupor. Earlier Continental authors, much of whose work was discussed by Jung and Carmichael,[6] claimed to have demonstrated functional rigidity or lack of responsiveness in the circulation of schizophrenic patients.

The mechanism of the observed clinical and physiologic changes is not established; Olkon [1] and many of the older authors [6] stressed the possibility of a structural change in the vascular tree, while Abramson and associates[5] and Jung and Carmichael[6] expressed the belief that vasoconstriction was the responsible factor. It was considered of interest, therefore, to test the effect on the acrocyanosis of schizophrenia of carbon dioxide, the capillary-dilating action of which is well known.

MATERIAL AND METHODS

Five experiments were made on 2 patients with the diagnosis of established schizophrenia; the patients were 22 and 46 years old and had been ill for eleven and fourteen years, respectively. Identical studies were also made on a depressed patient who did not exhibit acrocyanosis; the observations in this case served as a control.

In order to obviate the effects of discomfort and hyperventilation consequent to inhalation of carbon dioxide, the patients were given "intocostrin" intravenously in doses of 0.70 to 0.85 unit per pound (1.66 to 1.8 units per kilogram) of body weight. Approximately three minutes after the injection the patients became apneic, remaining so for ten to twenty minutes; after this, hiccuping began and during the next twenty minutes gradually passed over first into shallow breathing, then into normal respiration and finally into hyperventilation. Shortly before the onset of apnea the patients lost their cough and gag reflexes, and it was possible to insert a Magill catheter into the trachea through the nose without difficulty. This tube was in place by the time apnea began, so that administration of a mixture of 95 per cent oxygen and 5 per cent carbon dioxide could be started when necessary; the rate of administration of the gas mixture was maintained at approximately 6 liters per minute. The tracheal catheter was removed when cough and gag reflexes returned.

Samples of blood taken from an antecubital vein and a femoral artery were analyzed for oxygen and carbon dioxide contents by the method of Van Slyke

5. Abramson, D. I; Schkloven, N., and Katzenstein, K. H.: Peripheral Blood Flow in Schizophrenia and Other Abnormal Mental States: A Plethysmographic Study, Arch. Neurol. & Psychiat. **45**:973 (June) 1941.

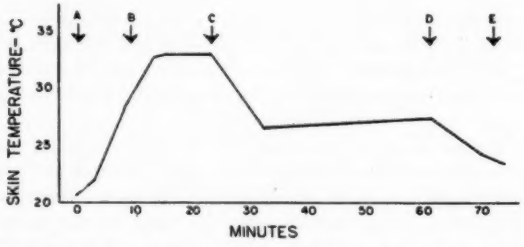
6. Jung, R., and Carmichael, E. A.: Ueber vasomotrische Reaktionen und Wormeregulation im katatonen Stupor, Arch. f. Psychiat. **107**:300, 1930.

and Neill,[7] slightly modified.[8] Samples were obtained before giving "intocostrin," during administration of the gas mixture and after withdrawal of the tube from the trachea. A thermocouple was used to measure the cutaneous temperature; measurements were made at intervals of two or three minutes. The temperature of the air in the room was between 15 and 20 C.

Gas Concentrations of the Blood, Expressed as Volumes Per Cent, and Cutaneous Temperatures*

	Before Inhalation of Carbon Dioxide	During Inhalation of Carbon Dioxide		After Inhalation of Carbon Dioxide
		Patient Apneic	Patient Breathing	
Arterial oxygen.....	18.86-22.36 (20.57)	19.45-22.54 (20.88)	19.70-20.94 (20.47)	21.34 †
Arterial carbon dioxide.....	42.25-45.34 (44.19)	50.80-58.60 (53.87)	46.01-50.70 (47.86)	44.80 †
Venous oxygen				
Schizophrenia.....	5.25-8.89 (7.13)	15.99-17.74 (16.91)	.....	6.75-10.65 (8.72)
Control.....	14.11 †	20.76 †	.....	.....
Cutaneous temperature of hand				
Schizophrenia.....	17.6-21.4 (20.4)	32.9-33.9 (33.2)	25.9-30.1 (28.2)	21.0-23.1 (21.8)
Control.....	30.2 †	32.2-33.1 †	.....	29.0 †

* Values in parentheses are average values.
† But one observation was made.



Effect of inhalation of a gas mixture containing 5 per cent carbon dioxide on the cutaneous temperature of a patient with schizophrenia.

At *A*, the oxygen content of arterial blood was 22.36 volumes, and the carbon dioxide content, 42.25 volumes, per cent; the oxygen content of venous blood was 8.89 volumes per cent. The patient was curarized; a tracheal tube was inserted, and insufflation of carbon dioxide and oxygen was begun.

At *B*, the oxygen content of arterial blood was 20.20 volumes, and the carbon dioxide content, 51.01 volumes per cent.

At *C*, there was return of respiration.

At *D*, the tube was removed; insufflation of carbon dioxide and oxygen was ended.

At *E*, the oxygen content of arterial blood was 21.34 volumes and the carbon dioxide content, 44.80 per cent; the oxygen content of the venous blood was 10.65 volumes per cent.

7. Van Slyke, D. D., and Neill, J. M.: The Determination of Gases in Blood and Other Solutions by Vacuum Extraction and Manometric Measurement, J. Biol. Chem. **61**:523, 1924.

8. Fieser, L. F.: A New Absorbent for Oxygen in Gas Analysis, J. Am. Chem. Soc. **46**:2639, 1924.

OBSERVATIONS

Before the administration of carbon dioxide was started, the hands of the schizophrenic patients were blue and the oxygen of the blood of the antecubital vein and the cutaneous temperatures were low. The former ranged from 5.25 to 8.89 volumes and averaged 7.13 volumes, per cent; the cutaneous temperature over the hand was between 17.6 and 21.4 C. (63.7 to 70.5 F.), averaging 20.4 C. (68.7 F.) (table, figure). The color of the skin and the oxygen content of the antecubital venous blood were normal in the control subject, and the cutaneous temperature was 30.2 C. (86.3 F.) During the period of administration of carbon dioxide the carbon dioxide of the arterial blood became elevated in all 3 subjects (table, figure), ranging from 46.01 to 58.60 volumes per cent; this change was associated with a rapidly progressive reddening of the skin of the entire body, especially over the hands and face. Capillary pulsations in the fingers became apparent and soon were pronounced. The cutaneous temperature rose progressively to from 32 to 34 C. (89.6 to 93.2 F.) in all subjects; when that level was reached, drenching generalized sweating began. The oxygen content of the antecubital venous blood in the schizophrenic subjects was at this time more than twice the control value; i. e., it was between 15.99 and 17.74 volumes per cent (table, figure). In the control subject the rise was smaller, since the initial level was not low. When the effect of the injected curare was wearing off, hyperventilation began. The carbon dioxide of arterial blood, the oxygen of venous blood and the cutaneous temperature all fell somewhat at this time (table). When the administration of carbon dioxide was discontinued, the hands of the schizophrenic subjects rapidly became cool and cyanotic, and the values for blood oxygen and cutaneous temperature returned toward their control levels. The rectal temperature remained unchanged during the period of study.

COMMENT

The finding of a low oxygen content of antecubital venous blood in schizophrenic patients is a reflection chiefly of diminished blood flow through the skin of the hands, since resting muscle has a very small blood flow [9] and the flow through the hands exceeds that through the fore-

9. (*a*) Grant, R. T., and Pearson, R. S. B.: The Blood Circulation in the Human Limb: Observations on the Differences Between the Proximal and Distal Parts and Remarks on the Regulation of Body Temperature, Clin. Sc. **3**:119, 1938. (*b*) Kunkel, P.; Stead, E. A., Jr., and Weiss, S.: Blood Flow and Vasomotor Reactions in the Hands, Forearm, Foot and Calf in Response to Physical and Chemical Stimuli, J. Clin. Investigation **18**:225, 1939.

arm.[10] Accordingly, the low values for the oxygen content of antecubital venous blood found here, in corroboration of the observations of earlier authors,[4] are an indication of stasis, largely in the skin of the hand. Conversely, the high oxygen values found during the period of administration of carbon dioxide (table, figure) are evidence of flow increased greatly above the normal. The observed changes in cutaneous temperature are in accord with the conclusion that cutaneous flow in the hand is greatly increased by inhalation of carbon dioxide; calculations from the data of Montgomery, Naide and Freeman[11] indicated that flow through the skin of the hands in the present experiments increased 500 per cent or more. In addition, the fact that venous blood became almost arterial in oxygenation at this time suggests that arteriovenous shunts became widely patent. Similarly, the occurrence of capillary pulsations indicates that at least the terminal arterioles dilated also.

It is important to note that the effects of hyperventilation were avoided in the present study. Although carbon dioxide is known to cause dilatation of capillaries,[12] observations made during inhalation of that gas by normal subjects revealed a decrease in blood flow in the hand[13]; this phenomenon is due not to the carbon dioxide per se but, rather, to neurogenic spasm[13e] consequent to hyperventilation.[14] In the present study, the effects of hyperventilation were prevented by curarization, and the action of carbon dioxide as a vasodilating agent

10. Abramson, D. I.: Vascular Responses in the Extremities of Man in Health and Disease, Chicago, University of Chicago Press, 1944, p. 80.

11. Montgomery, H.; Naide, M., and Freeman, N. E.: The Significance of Diagnostic Tests in the Study of Peripheral Vascular Disease, Am. Heart J. **21**: 780, 1941.

12. (*a*) Henderson, Y., and Harvey, S. C.: Acapnia and Shock: VIII. The Veno-Pressor Mechanism, Am. J. Physiol. **46**:533, 1918. (*b*) Hooker, D. R.: Evidence of Functional Activity on the Part of the Capillaries and Venules, Physiol. Rev. **1**:137, 1921. (*c*) McDowall, R. J. S.: The Effect of Carbon Dioxide on the Circulation: I., J. Physiol. **70**:301, 1930.

13. (*a*) Schneider, E. C., and Truesdell, D.: The Effects on the Circulation and Respiration of an Increase in the Carbon Dioxide Content of the Blood in Man, Am. J. Physiol. **63**:155, 1922. (*b*) Schneider, E. C.: A Study of Respiratory and Circulatory Responses to a Voluntary Gradual Forcing of Respiration, ibid. **91**: 390, 1929. (*c*) Gellhorn, E., and Steck, I. E.: The Effect of the Inhalation of Gases with a Low Oxygen and an Increased Carbon Dioxide Tension on the Peripheral Blood Flow in Man, ibid. **124**:735, 1938. (*d*) Sturup, G.; Bolton, B.; Williams, D. J., and Carmichael, E. A.: Vasomotor Responses in Hemiplegic Patients, Brain **58**:456, 1938. (*e*) Steck, I. E., and Gellhorn, E.: The Effect of Carbon Dioxide Inhalation on the Peripheral Blood Flow in the Normal and in the Sympathectomized Patient, Am. Heart J. **18**:206, 1939. (*f*) Abramson, D. I.: Vascular Responses in the Extremities of Man in Health and Disease, Chicago, University of Chicago Press, 1944, p. 170.

14. McDowall.[12c] Sturup and others.[13d]

was not inhibited. The mechanism whereby carbon dioxide causes cutaneous vasodilatation is not completely understood, but it is clear from the results of the present study that vasodilatation can occur in the cold, cyanotic hands of schizophrenic patients. These findings are in accord with the concept that the acrocyanosis of schizophrenia is consequent to vasoconstriction, a conclusion previously expressed by other authors. The latter include Jung and Carmichael,[6] who studied patients in catatonic stupor and found that warming of the skin of one part of the body gave rise to normal reflex vasodilatation over other parts. Similarly, Abramson and associates,[5] who found that the vascular response to direct warming or to a period of arterial occlusion was normal in schizophrenic patients with decreased blood flow in the hands, expressed the belief that vasoconstriction was responsible for the decreased flow observed. Further evidence in favor of this conclusion is the observation of Freeman [15] that vasodilatation in schizophrenic patients is normal after application of heat [15a] and during cyclopropane anesthesia.[15b] Jung and Carmichael [6] made the additional observation that the state of the circulation in the hands paralleled changes in clinical status.

It is unlikely that a generalized decrease in blood flow everywhere in the body is also a factor in the development of the changes in cutaneous color observed in patients with schizophrenia. As already pointed out, the blood flow is diminished in the hands but not in other parts of the limbs of patients with schizophrenia.[5] The statement made by Thompson and associates [4e] that the cardiac output may be somewhat low in persons with schizophrenia is difficult to evaluate, since detailed data were not presented by those authors. Other investigators,[16] using methods of doubtful accuracy for studying cardiac output, obtained contradictory results. The only published data on visceral circulation in schizophrenia are those bearing on blood flow in the brain, which is usually normal in this disease.[17] The fact that the

15. (*a*) Freeman, H.: Skin and Body Temperatures of Schizophrenic and Normal Subjects Under Varying Environmental Conditions, Arch. Neurol. & Psychiat. **42**:724 (Oct.) 1939; (*b*) Vaso-Dilatation in Normal and Schizophrenic Subjects During Cyclopropane Anesthesia, Psychosom. Med. **3**:170, 1941.

16. (*a*) Yde, A., and Bulow-Johansen, E.: Einige Betrachtungen über die Hämodynamik bei Schizophrenie, Acta psychiat. et neurol. **17**:207, 1942. (*b*) Faurbye, A., and Larsen, J. F.: The Circulation of the Blood in Schizophrenics: Estimated by Means of the Blood Pressure Method of Liljestrand and Zander, Acta psychiat. et neurol. **20**:159, 1945.

17. (*a*) Himwich, H. E.; Bowman, K. M.; Wortis, J., and Fazekas, J. F.: Biochemical Changes Occurring in the Cerebral Blood During the Insulin Treatment of Schizophrenia, J. Nerv. & Ment. Dis. **89**:273, 1939. (*b*) Wortis, J.; Bowman, K. M., and Goldfarb, W.: Human Brain Metabolism: Normal Values

(Footnote continued on next page)

circulation time is found to be normal in patients with schizophrenia [18] also points to the existence of normal cardiovascular dynamics in the body as a whole. Freeman's data,[19] showing a slow circulation time in some patients with schizophrenia, are discordant, unless his findings are the result of an unusual amount of vasoconstriction in the skin of some of his patients. Other authors have shown that pronounced cutaneous vasoconstriction induced in the arms of normal subjects may slow the arm to tongue or the arm to carotid circulation time,[20] even in the absence of any change in the circulation as a whole.

A number of authors [21] have reported low values for oxygen saturation of arterial blood in some patients with schizophrenia, and a similar observation has been made in our own laboratory.[22] The precise interpretation of these results is difficult, for some of the patients observed by us [22] held their breaths and others hyperventilated before and during arterial puncture; either phenomenon might lower somewhat the oxygen saturation of arterial blood. At any rate, the changes observed are too small to be important in the causation of the acrocyanosis of schizophrenia.

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and Values in Certain Clinical States, Am. J. Psychiat. **97**:552, 1940. (*c*) Gibbs, E. L.; Lennox, W. G., and Gibbs, F. A.: Bilateral Internal Jugular Blood: Comparison of A-V Differences, Oxygen-Dextrose Ratios and Respiratory Quotients, ibid. **102**:184, 1945. (*d*) Katzenelbogen, S.; Haws, R. J., and Snyder, R.: Biochemical Studies on Patients with Schizophrenia: Dextrose, Oxygen and Carbon Dioxide Contents of Arterial and Venous Blood from the Cranial Cavity, Arch. Neurol. & Psychiat. **51**:469 (May) 1944. (*e*) Rosenbaum, M.; Roseman, E.; Aring, C. D., and Ferris, E. B., Jr.: Intracranial Blood Flow in Dementia Paralytica, Cerebral Atrophy and Schizophrenia, ibid. **47**:793 (May) 1942. (*f*) Loman, J., and Myerson, A.: Circulation of the Brain and Face: Determinations of Oxygen and Sugar in Arterial and in Internal and External Jugular Venous Blood, ibid. **57**:94 (Jan.) 1947.

18. Finesinger, J. E.; Cohen, M. E., and Thomson, K. J.: Velocity of Blood Flow in Schizophrenia, Arch. Neurol. & Psychiat. **39**:24 (Jan.) 1938. Gottlieb, J. S.: Arm to Carotid Circulation Time in Abnormal Mental States, Arch. Neurol. & Psychiat. **41**:1117 (June) 1939. Wortis and others.[17b]

19. Freeman, H.: The Arm to Carotid Circulation Time in Normal and Schizophrenic Subjects, Psychiat. Quart. **8**:290, 1934; The Variability of Circulation Time in Normal and in Schizophrenic Subjects, Arch. Neurol. & Psychiat. **39**: 488 (March) 1938.

20. Stead, E. A., Jr., and Kunkel, D.: Influence of the Peripheral Circulation in the Upper Extremity on Circulation Time as Measured by the Sodium Cyanide Method, Am. J. M. Sc. **198**:49, 1939. Kvale, W. F., and Allen, E. V.: The Rate of the Circulation in the Arteries and Veins of Man: III. The Influence of Temperature of the Skin, Digestion, Posture and Exercise, Am. Heart J. **18**:546, 1939.

21. Segal and Hinsie.[4a] Thompson and others.[4e] Looney and Freeman.[4f]

22. Altschule, M. D.; Sulzbach, W. M., and Tillotson, K. J.: Effect of Electrically Induced Convulsions upon Respiration in Man, Am. J. Psychiat. **103**:680, 1947.

The cause of abnormal acral vasoconstriction which occurs with schizophrenia has not been established. It is common knowledge that lesser degrees of cyanosis of the hands may be observed in patients with other mental and emotional disorders; abnormal capillary structure is also well known to be present in patients with such conditions.[23] Vasomotor control is a complex process; cortical and hypothalamic influences have been shown to be important in the regulation of vasomotor tone[24]; the sympathetic nervous system is the pathway involved.[13d] It is pertinent that unpleasant emotion may cause arteriolar constriction and cooling in the hands of normal subjects[25] and of emotionally disturbed patients.[26] The role of venous spasm in the emotional vasomotor response which occurs in the limbs of

23. Schrijver-Hertzberger.[2] Suckow.[3] Deutsch, F.: Observations on the Capillaries of the Nailfold in Psychoneurotic Patients, Acta med. orient. **4**:327, 1945. Hauptmann, A.: Capillaries in the Finger Nail Fold in Patients with Neurosis, Epilepsy and Migraine, Arch. Neurol. & Psychiat. **56**:631 (Dec.) 1946. Cobb, S.; Cohen, M. E., and Badal, D. W.: Capillaries of the Nail Fold in Patients with Neurocirculatory Asthenia: Effort Syndrome, Anxiety Neurosis, ibid. **56**:643 (Dec.) 1946.

24. Abramson, D. I.: Vascular Responses in the Extremities of Man in Health and Disease, Chicago, University of Chicago Press, 1944, p. 18.

25. (*a*) Kunkel and others.[9b] (*b*) Montgomery and others.[11] (*c*) Sturup and others.[13d] (*d*) Freeman.[15b] (*e*) Yde and Bulow-Johansen.[16a] (*f*) Freeman, N. E.; Shaw, J. L., and Snyder, J. C.: The Peripheral Blood Flow in Surgical Shock: The Reduction in Circulation Through the Hand Resulting from Pain, Fear, Cold and Asphyxia, with Quantitative Measurements of the Volume Flow of Blood in Clinical Cases of Surgical Shock, J. Clin. Investigation **15**:651, 1936. (*g*) Wolff, H. G., and Mittelman, B.: Experimental Observations on Changes in Skin Temperature Associated with Induced Emotional States, Tr. Am. Neurol. A. **63**:136, 1937. (*h*) Burton, A. C.: The Range and Variability of the Blood Flow in the Human Fingers and the Vasomotor Regulation of Body Temperature, Am. J. Physiol. **127**:437, 1939. (*i*) Altschule, M. D.: Unpublished data, 1940. (*j*) Hertzman, A. B.: The Relative Responses of the Dorsal Metacarpal, Digital and Terminal Skin Arteries of the Hand in Vasoconstrictor Reflexes, Am. J. Physiol. **134**:59, 1941. (*k*) Neumann, C.; Cohn, A. E., and Burch, G. E.: A Study by Quantitative Methods of the Spontaneous Variations in Volume of the Tips of the Fingers and Toes and Posterior Superior Portion of the Pinna of Hypertensive and Senile Subjects, ibid. **136**:451, 1942. (*l*) Neumann, C.; Lhamon, W. T., and Cohn, A. E.: A Study of Factors (Emotional) Responsible for Changes in the Pattern of Spontaneous Rhythmic Fluctuations in the Volume of the Vascular Bed of the Finger Tip, J. Clin. Investigation **23**:1, 1944. (*m*) Burch, G. E.: A New Sensitive Portable Plethysmograph, Am. Heart J. **33**:48, 1947.

26. Mittelman, B., and Wolff, H. G.: (*a*) Affective States and Skin Temperature: Experimental Study of Subjects with Cold Hands and Raynaud's Disease, Psychosom. Med. **1**:271, 1939; (*b*) Emotions and Skin Temperature: Observations on Patients During Psychotherapeutic (Psychoanalytic Interviews), ibid. **5**:211, 1943.

normal subjects has also been stressed [27]; the changes in the hands are due both to arteriolar and to venous constriction, whereas those in the forearms are venous in origin.[27b] Warming inhibits emotional vasoconstriction in the hands of normal subjects.[27a] On the arterial side, apparently only the terminal cutaneous arteries, and not the radial, metacarpal and digital arteries, are involved in normal subjects [25]; on the other hand, Klingmann [28] described spasm of the radial arteries in schizophrenic patients. Ray and associates [29] recently showed how neurogenic vasoconstriction in the hands leads to accelerated deoxygenation of capillary blood and thereby causes cyanosis. Attempts to relate psychogenic vasoconstriction to specific types of emotion [26b] are not convincing.

The role of excessive secretion of epinephrine in the acral vasoconstriction of schizophrenia is probably not important. Although epinephrine constricts capillaries [30] and veins [31] and slows blood flow in the hands,[32] it has been shown by Fatheree and Allen [32c] that the effect of the substance is not striking in patients with a history of emotional acral vasoconstriction. Doses of epinephrine large enough to cause capillary and venous constriction also cause elevation of blood

27. (*a*) Capps, R. B.: A Method for Measuring Tone and Reflex Constriction of the Capillaries, Venules and Veins of the Human Hand with the Results in Normal and Diseased States, J. Clin. Investigation **15**:229, 1936. (*b*) Abramson, D. I., and Ferris, E. B., Jr.: Responses of the Blood Vessels in the Resting Hand and Forearm to Various Stimuli, Am. Heart J. **19**:541, 1940.

28. Klingmann, T.: Physical Signs in Schizophrenia, Am. J. Psych. **103**:69, 1946.

29. Ray, G. B.; Ray, L. H., and Johnson, J. R.: Factors Influencing Reduction Time of Blood in the Capillaries of the Skin, Am. J. Physiol. **147**:630, 1946.

30. Cotton, T. F.; Slade, J. G., and Lewis, T.: Observations upon Dermatographism, with Special Reference to the Contractile Power of the Capillaries, Heart **6**:227, 1916.

31. Crawford, A. C., and Twombly, M. M.: Notes on the Response of Veins to Epinephrine, New York State J. Med. **98**:327, 1913. Connet, H.: The Effect of Adrenalin on Venous Blood Pressure, Am. J. Physiol. **54**:96, 1920. Heimberger, H.: Ueber die Contractilität der kleinsten Venen, Ztschr. f. d. ges. exper. Med. **48**:179, 1925. Maloff, G.: Pharmakologische Versuche an isolierten Venen des Menschen, Arch. f. d. ges. Physiol. **229**:38, 1932. Budelmann, G.: Untersuchungen über den Venendruck, die Vitalkapazität der Lunge und das Herzminutenvolumen bei Gesunden und Herzkranken in Ruhe und bei Kreislaufbelastung, Ztschr. f. klin. Med. **127**:15, 1935. Iglauer, A., and Altschule, M. D.: The Effect of Paredrine on the Venous System, J. Clin. Investigation **19**:503, 1940.

32. (*a*) Smithwick, R. H.; Freeman, N. E., and White, J. C.: Effect of Epinephrine on the Sympathectomized Human Extremity: An Additional Cause of Failure of Operations for Raynaud's Disease, Arch. Surg. **29**:759 (Nov.) 1934. (*b*) Wilkins, R. W.; Weiss, S., and Haynes, F. W.: The Effect of Epinephrine in Circulatory Collapse Induced by Sodium Nitrite, J. Clin. Investigation **17**:41, 1938. (*c*) Fatheree, T. J., and Allen, E. V.: The Influence of Epinephrine on the Digital Arterioles of Man: A Study of the Vasoconstrictor Effects, ibid. **17**:108, 1938.

pressure; the arterial blood pressure in schizophrenic patients is usually not high. The fact that Smithwick and associates [32a] found that a sympathectomized extremity may exhibit emotional vasoconstriction does not establish circulating epinephrine as an important cause of this phenomenon in ordinary circumstances, for the sympathectomized limb is extremely hypersensitive to the action of epinephrine.

In addition to the direct effect of emotion on vasoconstrictor activity, it must also be borne in mind that if hyperventilation is present this, too, will result in vasoconstriction and diminution of blood flow in the hands,[13] but not in other parts of the extremities. Hyperventilation in patients with mental and emotional disorders is usually regarded as emotional in origin.

Direct evidence bearing on the origin of some types of acrocyanosis is afforded by the study of Day and Klingman [33] on acrocyanosis in an emotionally unstable child; their findings emphasize the role of cerebral factors in the occurrence of this disorder in cutaneous circulation. The portion of the cortex which influences vasomotor function is in the premotor area [34]; apparently, most of the area may influence vasomotor function, for no definite centers can be localized.[13d]

The mechanisms resulting in a change in cortical function which apparently gives rise to schizophrenic acrocyanosis are obscure. The degree of change seen in schizophrenic patients is usually more marked and more persistent than that seen in neurotic subjects or in normal persons who are experiencing unpleasant emotional states. This fact may be explained on the basis that the mental content of the schizophrenic patient is more distressing; on the other hand, it is possible that the reactivity of that portion of the cortex involved in vasoconstriction may be altered by changes within its cells. It must be remembered that vasomotor disturbances of various types may occur in patients with cortical lesions.[35] Studies on the effects of organic cortical lesions on vasomotor activity in animals are extensive; these have been reviewed by other authors.[36] There is general agreement that irritative lesions cause cutaneous vasoconstriction, whereas ablation results in vasodilatation; Lund [36b] showed that the vasomotor

33. Day, R., and Klingman, W. O.: The Effect of Sleep on Skin Temperature Reactions in a Case of Acrocyanosis, J. Clin. Investigation **18**:271, 1939.

34. Schwartz, H. G.: Effect of Experimental Lesions of the Cortex on the Psychogalvanic Reflex in the Cat, Arch. Neurol. & Psychiat. **38**:308 (Aug.) 1937.

35. (*a*) Kennard, M. A.; Viets, H. R., and Fulton, J. F.: The Syndrome of the Premotor Cortex in Man: Impairment of Skilled Movements, Forced Grasping, Spasticity and Vasomotor Disturbances, Brain **57**:69, 1934. (*b*) Abramson, D. I.: cited by Kennard, Viets and Fulton,[35a] p. 283.

36. (*a*) Schwartz.[34] (*b*) Lund, A.: The Function of the Cortical Vasomotor Centers Elucidated Through Experimental Studies on Animals, Acta psychiat. et neurol. **20**:213, 1945.

changes were limited to the skin and did not involve muscle. The work of Kennard [37] on monkeys is discrepant in that it records cutaneous vasoconstriction after premotor cortical ablation; on the other hand, Delgado and associates,[38] who also used monkeys, found that vasodilatation followed ablation. These differences possibly are to be accounted for by differences in the durations of the periods of observation employed. Available data afford no information bearing on the possibility that the premotor cortex of schizophrenic patients with acrocyanosis may be abnormal in function. On the other hand, there is no doubt as to the role of emotion in causing or exaggerating the acrocyanosis.

It is clear that many patients with schizophrenia exhibit abnormal vasoconstriction of the blood vessels of the hands. This condition is not observed constantly and is not specific for schizophrenia. It probably indicates a discomforting emotional state, and as such is useful in the clinical evaluation of patients. On the other hand, since these abnormally constricted vessels are normally responsive to factors such as warmth, which favor vasodilatation, the absence of pallor, cyanosis or coldness of the hands may be misleading.

The data of the present study show not only that the autonomic mechanisms responsible for vasomotion are normal in patients with schizophrenia but also that another autonomic mechanism, which governs sweating, is also normally responsive. Drenching sweat developed when the skin temperature reached 33 C. (91.4 F.), the level at which sympathetic sweating mechanisms are activated in normal subjects.[39]

The psychiatric literature contains many references to the concept that the circulation in schizophrenia is unresponsive or underresponsive to external stimuli. This concept has been used in various ways, i. e., as evidence of somatic as well as psychic withdrawal, or as evidence that schizophrenia is largely a disease of the autonomic nervous system, especially its chief center, the hypothalamus. As the present

37. Kennard, M. A.: Vasomotor Disturbances Resulting from Cortical Lesions, Arch. Neurol. & Psychiat. **33**:537 (March) 1935.

38. Delgado, J. M. R.; Fulton, J. F., and Livingston, R. B.: Stimulation of Area 13 and Skin Temperature Changes Following Its Ablation, Federation Proc. **6**:95, 1947.

39. Houghten, F. C., and Yagloglou, C. P.: Determining Lines of Equal Comfort, Tr. Am. Soc. Heat. & Vent. Engin. **29**:163, 1923. McSwiney, B. A.: The Composition of Human Perspiration, Proc. Roy. Soc. Med. **27**:839, 1934. Winslow, C. E. A.; Herrington, L. P., and Gagge, A. P.: Physiological Reactions of the Human Body to Varying Environmental Temperature, Am. J. Physiol. **120**:1, 1937. Hick, F. H.; Keeton, R. W., and Glickman, N.: Physiologic Response of Man to Environmental Temperature, Tr. Am. Soc. Heat. & Vent. Engin. **44**:145, 1938. Gurney, R., and Bunnell, I. L.: A Study of the Reflex Mechanism of Sweating in the Human Being: Effect of Anesthesia and Sympathectomy, J. Clin. Investigation **21**:269, 1942.

discussion shows, this concept receives no support from the data of physiologic studies: The vasomotor system of patients with schizophrenia is, if anything, hyperreactive, i. e., at least normally reactive in the direction of vasodilatation and overreactive in the direction of vasoconstriction. These conclusions are in harmony with those of Freeman [15a] and Cameron.[40] These physiologic phenomena become intelligible on the basis of the observation that a considerable amount of cutaneous vasoconstriction, apparently caused by cortical influences, may be present for long periods in spite of the absence of changes in the physical environment making for vasoconstriction; when, in addition, the skin is cooled even slightly by change in ambient temperature, the vasoconstriction which results may be extreme.

The present discussion is also pertinent in regard to one of the tenets of that branch of psychiatry known as "psychosomatic medicine," which holds that somatic physiologic changes caused by emotional, or at least functional, influences result after a time in organic change. Schizophrenia offers an example of functional change, i. e., pronounced cutaneous vasoconstriction, which may be present for several decades and may give rise to no resultant organic change in the parts involved; trophic changes in the skin do not occur, and the blood vessels retain their normal elasticity, as shown in the work cited here. On the other hand, it is of interest that emotional vasoconstriction apparently favors the development of damage in extremities subjected to prolonged exposure to severe cold.[41]

SUMMARY AND CONCLUSIONS

Administration of carbon dioxide causes disappearance of the acrocyanosis of schizophrenia. Dilatation of acral cutaneous capillaries, terminal arterioles and probably arteriovenous shunts occurs. The findings indicate that abnormal vasoconstriction apparently consequent, at least in part, to unpleasant emotional stimuli is responsible for the acrocyanosis which may occur in patients with schizophrenia. There is nothing to suggest the association of abnormal rigidity of the vascular system with this disorder. Acrocyanosis may be present over a period of several decades without loss of responsiveness of the vessels involved. Similarly, the findings do not support the view that a specific structural change is present in the vascular system of patients with schizophrenia.

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40. Cameron, D. E.: Heat Production and Heat Control in the Schizophrenic Reaction, Arch. Neurol. & Psychiat. **32**:704 (Oct.) 1934.

41. Osborne, J. W., and Cowen, J.: Psychiatric Factors in Peripheral Vasoneuropathy After Chilling, Lancet **2**:204, 1945.

PAROXYSMAL LACRIMATION (SYNDROME OF CROCODILE TEARS) AND ITS SURGICAL TREATMENT

Relation to Auriculotemporal Syndrome

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THE PHENOMENON of unilateral tearing during eating has been called paroxysmal lacrimation. According to legend, the crocodile was believed to weep hypocritical tears while devouring its victims; therefore Bogorad [1] termed the condition "syndrome of crocodile tears." This rare syndrome occurs oftenest as a sequel of facial nerve palsy. Ford [2] has shown that it cannot follow the commoner form of Bell's palsy, in which the lesion is distal to the geniculate ganglion; it can occur only in those cases in which the lesion is in or proximal to the ganglion. Moreover, the syndrome does not develop until the motor paralysis has disappeared. A theory of its mechanism has been described but not proved, and a permanent means of relief to patients having the syndrome has not been devised.

In this presentation, the theory is supported that the phenomenon is due to the misdirection of regenerating nerve fibers, and a surgical treatment for the condition is described. The surgical procedures employed in these cases resulted from our observation of the alteration in the tearing function which follows the surgical interruption of the greater superficial petrosal nerve in the treatment of unilateral headache.[3]

A review of the literature reveals but few instances of this phenomenon. Bogorad, in 1928, reported the first case of the syndrome

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From the Cleveland Clinic.

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1. Bogorad, F. A.: Symptom of Crocodile Tears, Vrach. delo **11**:1328-1330 (Sept.) 1928.

2. Ford, F. R.: Paroxysmal Lacrimation During Eating as Sequel of Facial Palsy: Syndrome of Crocodile Tears, Arch. Neurol. & Psychiat. **29**:1279-1288 (June) 1933.

3. Gardner, W. J.; Stowell, A., and Dutlinger, R.: Resection of Greater Superficial Petrosal Nerve in Treatment of Unilateral Headache, J. Neurosurg. **4**: 105-114 (March) 1947.

which followed facial nerve palsy. Kroll [4] cited a similar case in 1929, and Kaminsky,[5] 2 more cases in the same year. In 1933 Ford reported 4 cases and offered an interpretation of the syndrome which we believe to be correct. Russin [6] reviewed the literature up to 1939 and added 2 observations of his own. The same year Savin [7] noted 3 cases and Christoffel [8] 1. McGovern [9] reported a case in 1940. In 1942 Gottesfeld and Leavitt [10] treated a patient with the syndrome by an alcoholic injection into the sphenopalatine ganglion, thereby arresting the epiphora for four and one-half months. In 1936, although he did not present the histories, Tumarkin [11] mentioned 13 cases of the syndrome.

REPORT OF CASES

CASE 1.—A married white woman aged 47 came to the Cleveland Clinic in June 1946. She had been healthy until October 1943, when she began to have violent paroxysms of vertigo and vomiting, associated with ringing in the left ear. On July 8, 1944 Dr. Walter Dandy sectioned the left eighth nerve in the posterior fossa for relief of Ménière's disease. Immediately after the operation the left side of the face was paralyzed. The paralysis began to clear in six months and was replaced by spasms of the facial muscles. With the return of motor function, excessive lacrimation occurred in the left eye, and tears coursed down the cheek whenever she ate. The patient, being of sensitive temperament, complained that it was difficult for her to follow her occupation as a saleswoman because the involuntary facial contractions and epiphora elicited solicitous inquiries from her customers and associates.

The patient was well developed and well nourished. There was an increase in muscular tone in the left side of the face. The left nasolabial fold was deeper than the right, and the left palpebral fissure was narrower. Ticlike movements played about the left corner of the mouth when she winked the left eyelid; conversely, when the patient showed her teeth, the left eyelid partially closed. There was no demonstrable impairment of the sense of taste. Neither tear duct was obstructed.

4. Kroll, M.: Die neuropathologischen Syndrome, zugleich Differentialdiagnostik der Nervenkrankheiten, Berlin, Julius Springer, 1929, p. 222.

5. Kaminsky, S. D.: Ueber das Syndrom der Krokodils-Tränen, Deutsche Ztschr. f. Nervenh. **110**:151-160, 1929.

6. Russin, L. A.: Paroxysmal Lacrimation During Eating as Sequel of Facial Palsy: Syndrome of Crocodile Tears, J. A. M. A. **113**:2310-2311 (Dec. 23) 1939.

7. Savin, L. H.: Note on Three Cases Showing Crocodile Tears After Facial Paralysis, Brit. J. Ophth. **23**:479-482 (July) 1939.

8. Christoffel, H.: Verhinderung von Krokodilstränen durch Monokel, Schweiz. med. Wchnschr. **69**:455 (May 20) 1939.

9. McGovern, F. H.: Paroxysmal Lacrimation During Eating Following Recovery from Facial Paralysis: Syndrome of Crocodile Tears, Am. J. Ophth. **23**:1388-1389 (Dec.) 1940.

10. Gottesfeld, B. H., and Leavitt, F. H.: Crocodile Tears Treated by Injection into the Sphenopalatine Ganglion, Arch. Neurol. & Psychiat. **47**:314-315 (Feb.) 1942.

11. Tumarkin, I. A.: Some Aspects of Problem of Facial Paralysis, Proc. Roy. Soc. Med. **29**:1685-1691 (Oct.) 1936.

There was total deafness of the left ear. It was observed that shortly after she began to eat, tears would fill the conjunctival sac of the left eye and run down her cheek. Other forms of activity, including the act of chewing without food in her mouth, did not produce this reaction.

It was believed that the ticlike mass movements of the facial muscles in this case were due to the misdirection of regenerating motor fibers and that the lacrimation during eating was due, as suggested by Ford and Woodhall,[12] to the misdirection of efferent fibers to the lacrimal gland which were originally destined for the salivary gland. Since these misdirected regenerating fibers were presumed to pass through the greater superficial nerve, it was advised that this nerve be sectioned.

Operation.—Resection of the left greater superficial petrosal nerves was performed on July 5, 1946, with "pentothal" anesthesia. With the patient in the sitting position, through a linear incision, a small opening was made in the squamous portion of the temporal bone and the dura elevated from the floor of the middle fossa. The middle meningeal artery was controlled by a bit of cotton forced into the foramen spinosum, after which the middle meningeal vessels were divided and the dura was separated from the outer surface of the gasserian ganglion. The greater superficial petrosal nerve was readily identified running forward in its groove from the hiatus canalis facialis (fallopii) to a point medial to the foramen ovale, where it passed beneath the gasserian ganglion. The nerve was picked up on a nerve hook, divided at the hiatus canalis facialis and 1 cm. of the nerve resected. The middle meningeal vessels in the dura were then treated with the cautery, after which the wound was closed with tiers of buried interrupted black silk sutures.

The patient's recovery was uneventful. By the second postoperative day it was apparent that the tearing at mealtime had been abolished, and the patient was discharged from the hospital the following day. The patient was last seen on Aug. 15, 1947; there was at that time no return of her paroxysmal lacrimation. The ticlike movements of the face were unchanged.

Physiologic Observations on the Facial Nerve and Deductions Therefrom.—Krieg,[13] Ranson,[14] Chorobski and Penfield[15] and others have demonstrated several physiologic portions of the seventh nerve: 1. A motor component, the cells of which are in the motor nucleus of the facial nerve. These fibers run by way of the facial nerve to the superficial musculature of the face and scalp, the platysma muscle, the posterior belly of the digastric muscle and the stylohyoid muscle. 2. A sensory component, the cells of which are in the geniculate ganglion and which conveys gustatory impulses from the anterior

12. Ford, F. R., and Woodhall, B.: Phenomena Due to Misdirection of Regenerating Fibers of Cranial, Spinal and Autonomic Nerves: Clinical Observations, Arch. Surg. **36**:480-496 (March) 1938.

13. Krieg, W. J. S.: Functional Neuroanatomy, Philadelphia, The Blakiston Company, 1942.

14. Ranson, S. W.: The Anatomy of the Nervous System from the Standpoint of Development and Function, ed. 7, Philadelphia, W. B. Saunders Company, 1943.

15. Chorobski, J., and Penfield, W. Cerebral Vasodilator Nerves and Their Pathway from Medulla Oblongata, Arch. Neurol. & Psychiat. **28**:1257-1289 (Dec.) 1932.

two thirds of the tongue and proprioceptive impulses from the face to the tractus solitarius. 3. An antonomic-parasympathetic component originating in the cells of the nucleus salivatorius superior. This autonomic component distributes secretory and vasodilatory fibers to the submaxillary and sublingual glands by way of the nerve of Wrisberg (nervus intermedius), the chorda tympani and the lingual nerve, as well as to the lacrimal gland [16] by way of the nerve of Wrisberg, the greater superficial petrosal nerve, the vidian nerve (nerve of the pterygoid canal) and the sphenopalatine ganglion. The autonomic component has other functions, which are not pertinent to the present discussion.

Proximal to the geniculate ganglion all the components of the facial nerve are contiguous. Distal to the ganglion the fibers disperse. In the preceding case, the lesion was undoubtedly of the intracranial portion of the nerve, where all the components are adjacent. If Spiller [17] and, later, Ford and Woodhall [12] were correct in their theory that regenerating nerve fibers may become misdirected, one can readily appreciate how some of the parasympathetic efferent fibers which formerly ran in the chorda tympani and the lingual nerve to the submaxillary and sublingual glands had entered the greater superficial petrosal nerve, ultimately to reach the lacrimal gland. Thus, through this misrouting of secretory impulses, the patient lacrimated whenever a gustatory stimulus was evoked. Section of the greater superficial petrosal nerve interrupted the efferent arm of the reflex, and the paroxysmal tearing was prevented.

The foregoing anamnesis is comparable to that in all cases of the syndrome of crocodile tears described in the literature up to the present time; that is, the condition follows palsy of the facial nerve. In the next 2 cases the syndrome developed without a preceding facial palsy and as a late sequel to the very operation which relieved the condition in the first case, namely, a resection of the greater superficial petrosal nerve.

Case 2.—A white man aged 53 entered Cleveland Clinic on Dec. 23, 1946. He previously had had an intracranial ligation of the left middle meningeal artery in June 1944 for attacks of intense left hemicrania, and on March 3, 1945 a section of the left greater superficial petrosal nerve had been done via the same route in treatment for a recurrence of the attacks. Both procedures afforded him some, though not permanent, relief. His present complaint was recurrence of unilateral headaches, which had been occurring one to three times per twenty-four hours, day or night, for the past week and lasting one-half to one and one-half hours. Each bout was accompanied with excessive lacrimation of the left eye. The patient said that the pain was unbearable and that something would have to be done to

16. Landolt, H.: Ueber die Innervation der Thränendrüse, Arch. f. d. ges. Physiol. **98**:189-216, 1903.

17. Spiller, W. G.: Contracture Occurring in Partial Recovery from Paralysis of Facial Nerve and Other Nerves, Arch. Neurol. & Psychiat. **1**:564 (May) 1919.

afford him relief. He stated that several months after his operation, in March 1945, his left eye began to tear profusely whenever he ate, the tears often running down his cheek. Neither side of his face had ever been paralyzed. The physical and neurologic status was essentially normal.

The occurrence of crocodile tears in this case could not be explained as readily as in the preceding one, since the greater superficial petrosal nerve, which was presumably the site of the lesion, contains no salivary fibers which could become misdirected to the lacrimal gland. The neighboring lesser superficial petrosal nerve, a branch of the ninth nerve, however, does carry salivary fibers.[13] Furthermore, this nerve pursues a course parallel to the greater superficial petrosal nerve, and just a few millimeters lateral to it in the middle cranial fossa, and, therefore, is included in every resection of the greater superficial petrosal nerve. It was assumed, therefore, that in this case the secretory fibers regenerating from the central end of the lesser superficial petrosal nerve had become misdirected and had grown into the peripheral end of the greater superficial petrosal nerve. With this clinical evidence of malfunction of the ninth nerve, it was considered possible that the unilateral headache might be on a similar basis, and a resection of the ninth nerve in the posterior fossa was advised. This was done Dec. 30, 1946, and the patient has experienced neither headache nor paroxysmal tearing up to the time of this report.

Case 3.—A white man aged 37 was admitted to Cleveland Clinic on March 21, 1945, with the chief complaint of having had, for the preceding five months, bouts of intense, sharp unilateral pain, beginning in the left temple and spreading to the left eye and to the supraorbital and postauricular region on that side. At first he had about one attack a week, each episode lasting from twenty to thirty minutes; but for the past several weeks he had been having the pain every two or three days in a more intensified form, lasting forty-five to sixty minutes. He stated that with each episode of pain the left eye would tear profusely and a watery secretion would drip from his left nostril. The physical and neurologic status was normal.

Our experience had shown that this type of headache could usually be relieved by resection of the greater superficial petrosal nerve,[8] and therefore this operation was advised. On April 11, 1945, through the usual temporal approach, the left middle meningeal artery and the greater superficial petrosal nerve were divided. The patient recovered without incident.

The frequency and intensity of the unilateral headaches were mitigated to the extent that the patient could endure them, and they were no longer accompanied with lacrimation. However, four or five months after the operation, he became annoyed with a low grade pain which was referred to the left eye and temple whenever he ate, accompanied with a copious overflow of tears down his cheek from the left eye. Shortly thereafter a thin, watery fluid would drip from his left nostril. This was distressing and necessitated wiping his cheek and blowing his nose numerous times during each meal. In February 1947, the left-sided headaches became more frequent and severer, and the patient again sought relief. Again, it was believed that the "crocodile tears" and associated hemicrania might be due to a misrouting of regenerated autonomic nerve fibers after surgical resection of the greater and lesser superficial petrosal nerves. On the basis of our successful experience in case 2, division of the left glossopharyngeal nerve was advised. This was done on March 10, 1947. As soon as the patient began to eat after the operation, it was apparent that the paroxysmal tearing and nasal dripping had been abolished. When he was last seen, on June 12, 1947, there was no recurrence of the epiphora, and he stated that the intensity of the hemicrania had diminished 75 per cent. There was some residual aching in the region of the left temple, which he could endure.

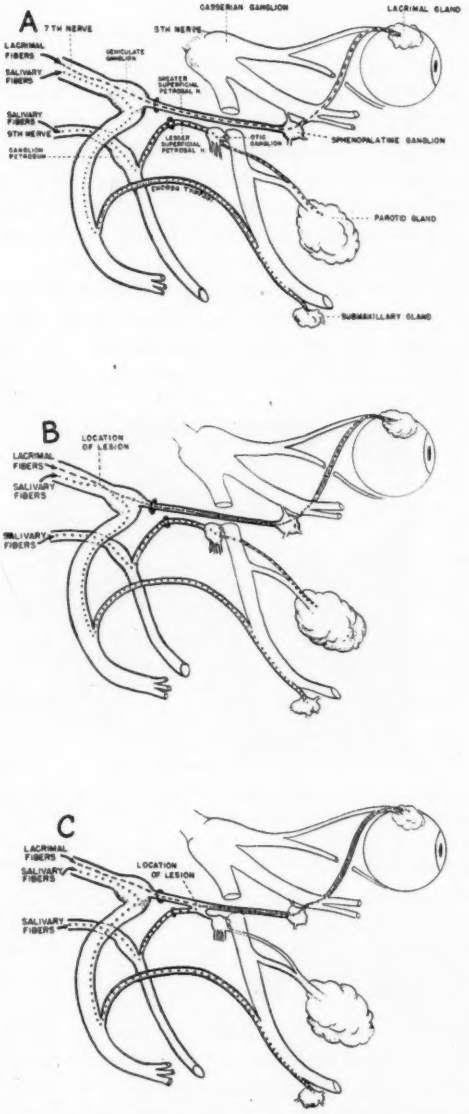


Fig. 1.—*A*, normal pathways for lacrimal and salivary efferent fibers. The salivary fibers of the seventh nerve go to the submaxillary gland, and those of the ninth nerve, to the parotid gland. *B*, location of the lesion (surgical trauma) in case 1. The drawing indicates the course of the aberrant salivary fibers reaching the lacrimal gland, in company with normal lacrimal efferent fibers. *C*, manner in which salivary fibers in the lesser superficial petrosal nerve become shunted into the greater superficial petrosal nerve to reach the lacrimal gland, as in cases 2 and 3.

PHYSIOLOGIC OBSERVATIONS

In case 1, and all cases heretofore reported, the phenomenon of crocodile tears occurred as a sequel of facial palsy. In neither of the last 2 cases presented was there a facial palsy; yet the syndrome was evident in both as a delayed complication following resection of the greater superficial petrosal nerve. In order to explain this phenomenon, it is necessary to consider the anatomic and physiologic properties of the glossopharyngeal nerve, together with its distribution and relations to certain components of the facial nerve.

Ranson,[14] Krieg[13] and others have shown that the ninth nerve contains: (1) a motor component, the cells of which are in the nucleus ambiguus and supply the stylopharyngeus muscle; (2) a sensory component, the cells of which are in the ganglion petrosum and convey

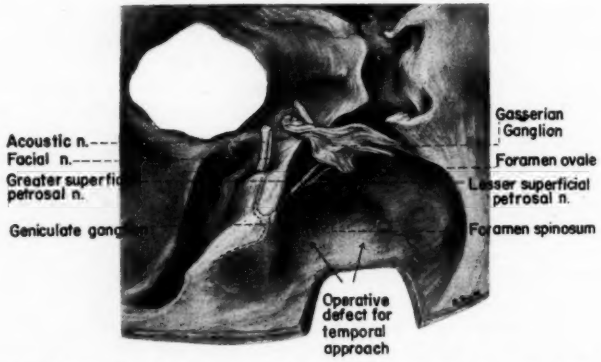


Fig. 2.—Schematic view of the middle fossa, showing the proximity of the lesser and greater superficial petrosal nerves in their intracranial course.

gustatory impulses from the posterior third of the tongue and general sensory impulses from the pharynx and the posterior third of the tongue to the tractus solitarius, and (3) an autonomic-parasympathetic component, originating in the cells of the inferior salivatory nucleus. This autonomic component distributes secretory and vasodilatory fibers to the parotid gland by way of the glossopharyngeal nerve and its tympanic branch (Jacobson's nerve), the lesser superficial petrosal nerve, the otic ganglion and the auriculotemporal nerve. It is this autonomic portion of the glossopharyngeal complex which concerns us here.

As the lesser and greater superficial petrosal nerves emerge from the petrous portion of the temporal bone, they lie but a few millimeters apart and traverse the middle fossa along its floor in close proximity until the lesser superficial petrosal nerve leaves through the foramen ovale (fig. 2). If both these preganglionic parasympathetic nerves are

divided, as was done in cases 2 and 3, it is possible that on regeneration some of the secretory fibers in the lesser superficial petrosal nerve destined for the parotid gland might find their way into the distal segment of the greater superficial petrosal nerve and form connections with the lacrimal gland. By means of this aberration a gustatory stimulus evoked lacrimation in cases 2 and 3. This theory was proved, since division of the ninth nerve, which carries salivary but no lacrimal efferent fibers, eliminated the paroxysmal tearing in both cases.

Obviously, redividing the greater superficial petrosal nerve in cases 2 and 3 would have arrested the paroxysms of tearing, just as it did in case 1; but this procedure might have been followed again by a similar misdirection of the regenerating fibers. It was believed that if the ninth nerve was divided in the posterior fossa there was no likelihood of recurrence of the tearing. Furthermore, since the chief complaint of both patients was not epiphora but headache, it was thought that perhaps the misrouting of autonomic nerve fibers was also responsible for the head pain, which could be alleviated by dividing the glossopharyngeal nerve. Fortunately, this procedure proved successful in 1 case, and partly so in the other.

RELATIONS TO AURICULOTEMPORAL SYNDROME

In many respects, the auriculotemporal syndrome is similar to the syndrome of paroxysmal lacrimation just described. The condition occurs as a sequel to suppurative parotitis, penetrating wounds and surgical procedures about the parotid gland which injure the auriculotemporal nerve. In this syndrome, when the patient eats, the skin over the parotid area becomes erythematous and droplets of sweat form on it, often in sufficient quantity to run down the cheek. The basis for this strange phenomenon is analogous to that which results in the syndrome of crocodile tears, namely, misdirecting of regenerating autonomic nerve fibers.

The auriculotemporal nerve is a branch of the third division of the trigeminal nerve. Before entering the substance of the parotid gland, it receives secretory and vasomotor fibers for the sweat glands from the cervical portion of the sympathetic system, and parasympathetic secretory and vasodilatory fibers derived from the glossopharyngeal nerve by a communication received from the otic ganglion and the lesser superficial petrosal nerve. The fibers in this instance are postganglionic.

A lesion of the auriculotemporal nerve immediately distal to the point where it receives its autonomic branch from the otic ganglion can result in misdirecting of regenerating parasympathetic fibers. Thus, some secretory and vasodilatory nerve fibers which originally supplied the parotid gland become misrouted to form connections with the arterioles of the skin and sweat glands. As a result, when a

gustatory stimulus is evoked, paroxysmal sweating and vasodilatation occur in the distribution of the auriculotemporal nerve. Presumably, division of the glossopharyngeal nerve in the posterior fossa would abolish this syndrome also, for the secretory and vasodilating efferent impulses which originate in the inferior salivatory nucleus leave by the ninth nerve. These two syndromes are, therefore, related only in that both are due to misdirecting of regenerating autonomic nerve fibers.

SUMMARY

In a case of paroxymal lacrimation occurring during eating caused by surgical trauma to the intracranial portion of the facial nerve, relief was obtained by resection of the greater superficial petrosal nerve. In 2 additional cases of this syndrome resulting from surgical trauma to the greater and lesser superficial petrosal nerves, relief followed resection of the glossopharyngeal nerve. These operative procedures are based on sound physiologic and anatomic principles.

The surgical relief obtained in these cases furnishes proof for the theory that the syndrome is caused by misdirection of regenerating salivary fibers.

The auriculotemporal syndrome is related to paroxysmal lacrimation only in that both are caused by misdirecting of regenerating autonomic nerve fibers.

The Cleveland Clinic.

MENINGOSARCOMA WITH PULMONARY METASTASIS

Report of a Case

ALVIN J. SWINGLE, M.D.
WOOD, WIS.

A REVIEW of the literature on meningioma and meningosarcoma reveals only 1 reported case of metastasis to the lungs. This was the case of Dorothy Russell, reported by Cushing and Eisenhardt [1] (1938), in which pulmonary metastases were observed at necropsy. The purpose of the present paper is to report a second case of meningosarcoma with pulmonary metastasis.

HISTORICAL REVIEW

Since the time of Antoine Louis [2] (1774), who wrote on fungating tumors of the dura mater, differences of opinion have been expressed by pathologists, chiefly with respect to the theories of origin, pathogenesis and terminology of meningeal tumors. The embryologists have contributed to the general disagreement by their changing concepts of the derivation of the cells forming the coverings of the central nervous system. During the nineteenth century Cruveilhier [3] (1829-1835) and Lebert [4] (1845), in France; Paget [5] (1854), in England, and Meyer [6] (1860) and Virchow [7] (1847), in Germany, made the greatest contributions to the increasingly accepted concept of the mesothelial origin of

From the Department of Pathology, Veterans Hospital, Wood, Wis., and the Marquette University School of Medicine.

Published with permission of the Medical Director, Veterans Administration, who assumes no responsibility for the opinions expressed or conclusions drawn by the authors.

1. Cushing, H., and Eisenhardt, L.: Meningiomas, Springfield, Ill., Charles C Thomas, Publisher, 1938, p. 692.

2. Louis, A.: Mémoire sur les tumeurs fongueses de la dure-mère, Mém. Acad. de chir. **5**:1-59, 1774.

3. Cruveilhier, J.: Anatomie, pathologique du corps humain, Paris, J. B. Baillière & fils, 1829, vol. 1, p. 8.

4. Lebert, H.: Physiologie pathologique, ou recherches cliniques, Paris, J. B. Baillière, 1845, vol. 2.

5. Paget, J.: Lectures on Surgical Pathology, Philadelphia, Lindsay & Blakiston, 1854, p. 699.

6. Meyer, L.: Ueber die Bedeutung der pacchionischen Granulationen, Virchows Arch. f. path. Anat. **19**:171-188, 1860.

7. Virchows, R.: Zur Entwickelungsgeschichte des Krebses, Virchows Arch. f. Path. Anat. **1**:197, 1847.

tumors of the meninges. The dawn of the twentieth century found Engert [8] (1900) distinguishing four types of meningiomas, with Bailey and Bucy,[9] in 1931, elaborating this classification to nine distinct histologic types, to which they later added a tenth. In 1938 Cushing and Eisenhardt,[10] in the monumental work entitled simply "Meningiomas," reviewed a century and a half of progress toward the present day concept of these tumors. They based their classification on Bailey's but distinguished several variations under each type.

CLASSIFICATION

The classification set up by Bailey and Bucy [9] included nine types based on the histologic characteristics of the tumor and the theory that the leptomeninx is the point of origin: (1) mesenchymal, (2) angioblastic, (3) meningotheliomatous, (4) psammomatous, (5) osteoblastic, (6) fibroblastic, (7) melanoblastic, (8) sarcomatous and (9) lipomatous. They concluded that all were of connective tissue nature.

Hsü,[11] in 1940, elaborated on and classified meningosarcomas, describing four types: (1) sarcomatosis, (2) alveolar sarcoma, (3) fibrosarcoma and (4) perithelial sarcoma; he concluded that such tumors must arise from leptomeningeal tissue either over the surface of the brain or around its blood vessels, the site of origin accounting for certain peculiarities. All are of connective tissue nature, must be derived from leptomeningeal tissue and may differentiate toward meningothelial cells, with no reticulin formation, or toward fibroblasts, with reticulin formation.

REPORT OF CASE

History.—H. A. B. was originally admitted to the Veterans Hospital, Wood, Wis., on Aug. 6, 1932, at the age of 39 for repair of an inguinal hernia. He complained also of frontal headache of two month's duration and weakness of the left leg. The physical condition at this time was normal, except for a large inguinal hernia on the left side and unequal knee jerks, the left being stronger than the right. He was discharged after surgical repair of the hernia.

The headache persisted, was frontal and continuous and became severer at night. Numbness of the left arm and leg produced a staggering gait to the left. On his readmission, on Feb. 7, 1933, there was a suggestion of weakness of the left side of the face; the patient tended to "throw" the left foot when walking; the left knee jerk was more active than the right; the Babinski sign was elicited on the left side, and the abdominal reflexes and the left cremasteric reflex were absent. There was bilateral choked disk, measuring 1.5 to 2.0 D. on the right and 4.0 D. on the left; vision was 20/30 in each eye, and there was

8. Engert, F.: Ueber Geschwülste der Dura mater, Virchows Arch. f. Path. Anat. **160**:19-32, 1900.

9. Bailey, P., and Bucy, P. C.: The Origin and Nature of Meningeal Tumors, Am. J. Cancer **15**:15-54, 1931.

10. Cushing and Eisenhardt,[1] p. 31.

11. Hsü, Y. K.: Primary Intracranial Sarcomas, Arch. Neurol. & Psychiat. **43**:901-924 (May) 1940.

no hemianopsia. A roentgenogram of the skull revealed nothing abnormal. The patient was transferred to Hines General Hospital for treatment of a tumor of the brain.

The past history was essentially noncontributory except for a head injury ten to twelve years before.

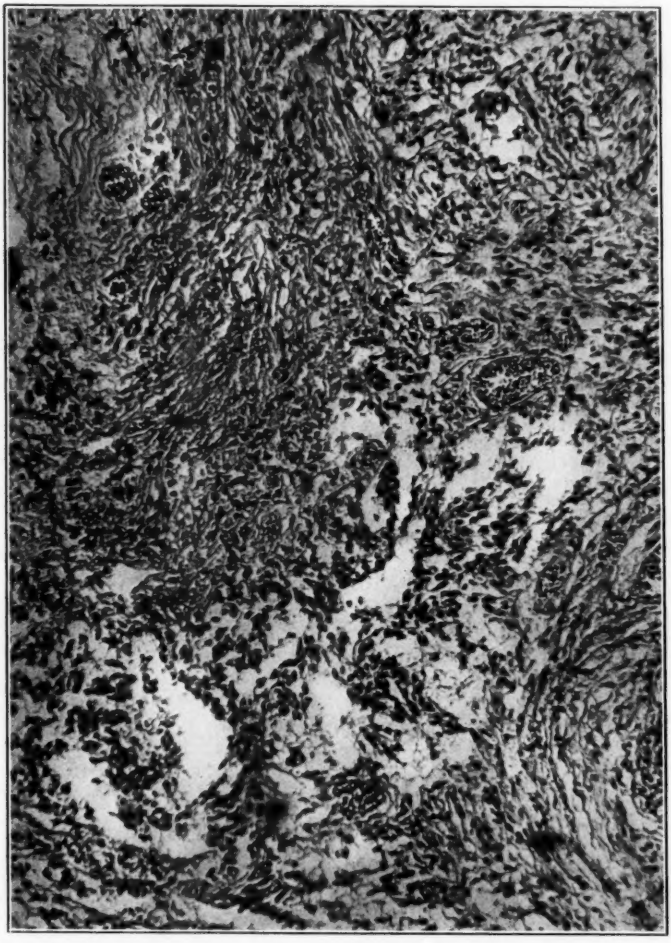


Fig. 1.—Tumor as seen at autopsy, showing interlacing bundles of fibroblast-like cells around and between blood vessels. Hematoxylin and eosin; × 60.

Clinical Course.—At operation, on May 2, 1933, a large, circumscribed tumor, described by the surgeon as a typical meningioma, was observed lying against the falx cerebri on the right. It was so extensive that the attachment to the dura had to be left for fear of injuring the longitudinal sinus.

Except for monthly jacksonian seizures, which were controlled by sedatives, the patient was comparatively well until Oct. 6, 1941, when he reentered the hospital. A decompression was done on Jan. 6, 1946, at which time part of the recurrent tumor was removed in pieces. When the patient was discharged on March 22, 1942, there was left homonymous hemianopsia with bilateral blurring

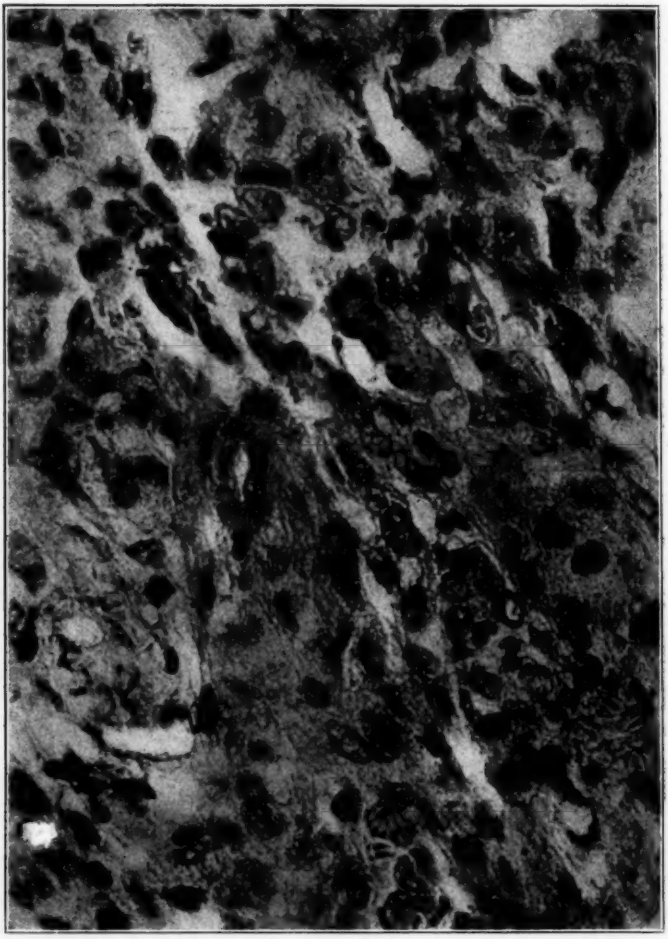


Fig. 2.—Higher magnification of a portion of the section in figure 1, showing the cell type of the primary tumor. Hematoxylin and eosin; × 325.

of the nasal margins, and a mass the size of a plum protruded from the decompressed area in the right occipitoparietal region. In August 1942 there was recurrence of jacksonian seizures, with clonic convulsions of the left side of the body and loss of control of the bladder sphincter. The mass in the right occipitoparietal region continued to enlarge, and vision gradually became worse. He

again entered the hospital on Dec. 29, 1942, with marked progression of all symptoms. His gait was then spastic on the left, and there were incoordination and impairment of deep position sense. In February 1943 he was given high voltage roentgen therapy (6,000 r), with no improvement. After this he became almost completely vegetative and lost about 100 pounds (45 Kg.) in weight. A persistent cough was present from November 1944 on. On Oct. 14, 1946 he began to run a fever; fluid developed in both lung fields, and he died on October 16.

Autopsy.—The general pathologic diagnosis was bronchopneumonia of the lower lobes of both lungs; generalized arteriosclerosis with coronary sclerosis; brown atrophy of the myocardium; chronic, adhesive pleuritis on the right;

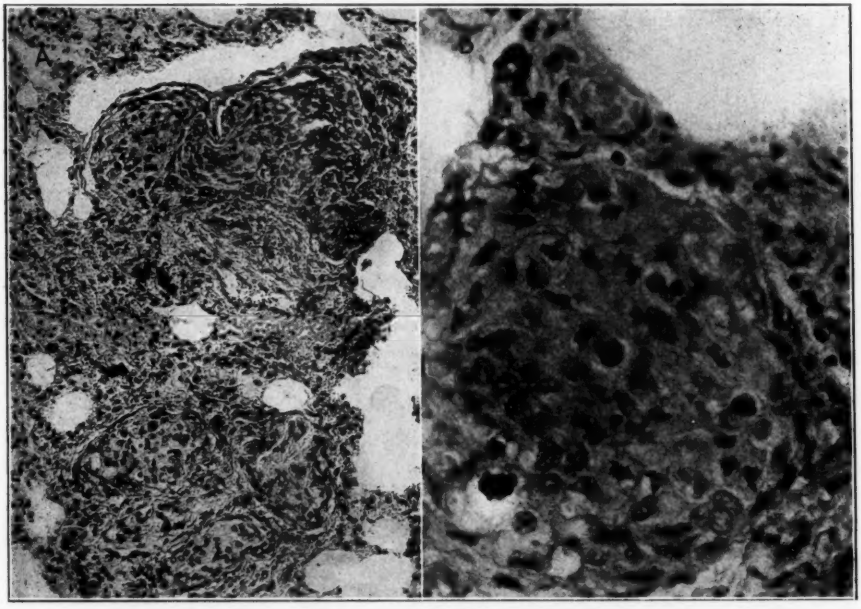


Fig. 3.—*A*, two small nodules in the lung identical with the primary tumor in the brain. Hematoxylin and eosin; × 60. *B*, tumor nodule in the lung, showing the spindle-shaped cell type, corresponding to the cell type in the primary tumor. Hematoxylin and eosin; × 325.

parenchymatous degeneration of the internal organs; benign, minimal hypertrophy of the prostate; status following an old craniotomy; localized external hydrocephalus; cerebral edema, and meningosarcoma with microscopic metastases to the lung.

In the right occipitoparietal area of the skull there was an irregular craniotomy wound, measuring 12 by 7 cm., through which protruded a cystic mass containing 350 cc. of a clear, light yellow fluid. Medial to the cyst, in the occiput of the right hemisphere, was a tumor measuring 12 cm. in all directions and extending over the midline into the left hemisphere. It was yellowish gray, with many areas of hemorrhage and necrosis. The tumor tissue showed a uniform grittiness. There was gross extension of the tumor by contiguity to the skull

and scalp. The remainder of the brain showed the effects of increased intracranial pressure, as evidenced by flattening of the convolutions, dull, brownish-gray discoloration of the cortex, flattening of the right lateral ventricle and dilatation of the left lateral ventricle.

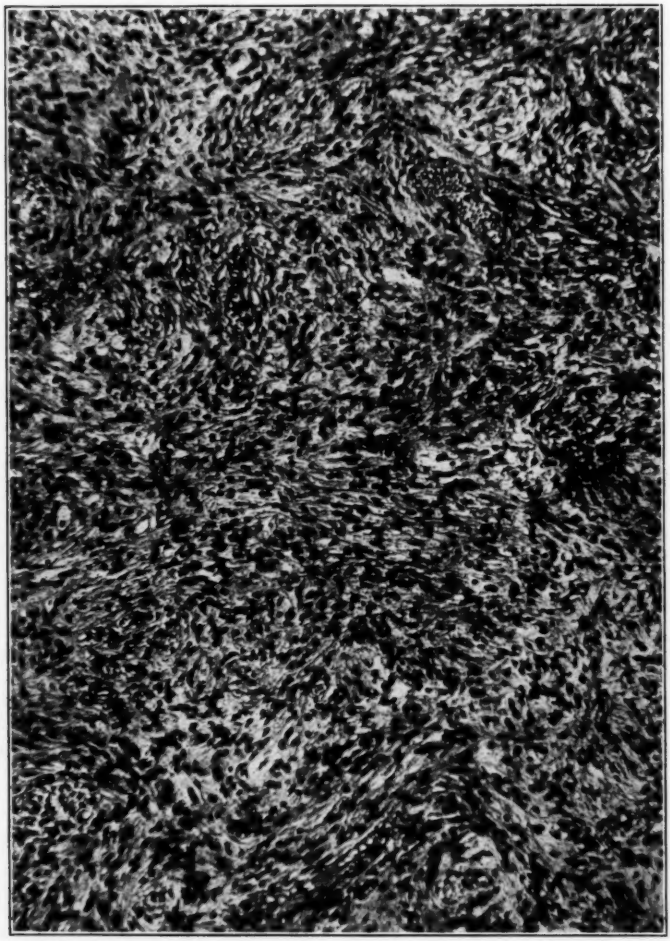


Fig. 4.—Tumor removed in 1933, showing essentially the same histopathologic picture as the tumor at autopsy. Hematoxylin and eosin; × 60.

The microscopic examination was of interest only with respect to the tumor and lungs. The tumor showed a fairly uniform structure, with some variations (fig. 1). There was an abundance of blood vessels, around which the tumor cells alined themselves in a definite onion shell pattern. The tumor showed considerable degeneration. In some areas there was hyalinization with cholesterol

slits. The involved capillaries showed considerable thickening and hyalinization. The tumor cell was rather large, pale and elliptic with a large nucleus (fig. 2). Nucleoli were absent, and the cytoplasm merged in a syncytial pattern. In scattered areas some cells were slightly larger and darker staining than in others. There were vacuoles in the cytoplasm of some cells, which proved to be fat when stained scarlet red. Stains for reticulum showed a dense network, particularly in the perivascular areas. The Van Gieson stain showed only streaks of fibrous tissue, and to a minor degree. Mallory's phosphotungstic acid hematoxylin stain showed intracellular fibrous tissue projecting through the tail of each cell, but a scanty deposit of strands.

Sections of the lung showed obvious bronchopneumonia with a heavy infiltration of polymorphonuclear leukocytes into the alveoli and bronchi. In a portion of the lung not involved in the pneumonic process there were small nests of cells which were large, pale and pinkish staining, with spindle-shaped, vesicular nuclei (fig. 3 *A* and *B*). These cells were identical with the "fibroblast-like" cell of the primary tumor in the brain.

A review of a microscopic section of the tumor removed surgically in 1933 showed it to be identical with the autopsy specimen (fig. 4). It was perhaps of not quite so loose a texture but presented the same cell type and the same general architecture.

COMMENT

Meningosarcoma is considered of rare occurrence and metastasis even rarer. Grinker [12] (1934) stated that sarcomas of leptomeningeal origin do not metastasize, and Cushing and Eisenhardt [13] asserted that they rarely, if ever, metastasize. The usual age of occurrence (clinically) is 40 to 50. The question of trauma as an etiologic factor is a moot one, Ewing [14] expressing doubt that it plays a part and Cushing [13] stating with certainty that it does. In the present case the clinical onset was at the age of 39, with a history of trauma ten to twelve years before. Grossly and historically, the tumor fulfils all the requirements for a diagnosis of sarcoma in that it recurred after removal; was invasive, having spread to the opposite hemisphere, the skull and the scalp, and did not change its histologic appearance during its course. According to Bailey [15] and Hsü, a sarcoma in the intracranial cavity arises from the leptomeninx, is of connective tissue type and is invasive. Histologically this tumor was of connective tissue type and was definitely invasive. It flourished around blood vessels and degenerated between them.

Other possible explanations for the tumor cells seen in the lung must be considered. 1. That the tumor is primary in the lung with

12. Grinker, R. R.: Neurology, Springfield, Ill., Charles C Thomas, Publisher, 1934, p. 502.

13. Cushing, and Eisenhardt,[1] p. 29.

14. Ewing, J.: The Modern Attitude Toward Traumatic Cancer, Bull. New York Acad. Med. **11**:281-333, 1935.

15. Bailey, P.: Proceedings of 1943 Tumor Seminar of the American Society of Clinical Pathology on Intracranial Tumors, Am. J. Clin. Path. **13**:464-496 and 553-564, 1943.

metastasis to the brain can be dismissed on the basis of the history and the absence of pulmonary signs over a long period of years. The morphologic and histologic features of the tumor are inconsistent with primary pulmonary carcinoma. 2. That it is an independent tumor developing coincidentally in the lung is a definite possibility. Primary sarcoma of the lung is extremely rare (Ewing [16]), being associated with tuberculosis, syphilis or chronic suppuration in most cases in the literature and appearing to have been a form of productive or organizing pneumonia in others. However, histologically, this picture does not fit any of the described cases of primary sarcoma of the lung. 3. That it is metastatic from the intracranial tumor seems most likely. The fact that only 1 such case of pulmonary metastasis has been reported does not militate against this theory. It is reasonable that sarcoma of the meninges should metastasize, since sarcomas everywhere else in the body are known to do so. This case and the case reported by Cushing are similar in their long, clinical courses, with the repeated surgical intervention and terminal picture. In both cases metastases were discovered at autopsy and were apparently of very recent or terminal occurrence. The very vascularity of these tumors, with their tendency to grow along blood vessels and their predilection to hemorrhage and necrosis, should make a hematogenous spread by vascular emboli of tumor cells a most likely possibility. It is probable that if patients with this tumor were to live long enough, with their illness pursuing a course similar to the present one, more would eventually present metastases.

For the reasons outlined in this paper, it is concluded that this meningosarcoma should be classified as a fibrosarcoma of leptomeningeal origin with terminal pulmonary metastasis.

SUMMARY

1. The past work leading up to the present day concept of the origin and nature of meningeal tumors is briefly summarized.

2. A brief résumé of the classification of meningiomas in general, as outlined by Bailey and Bucy, and of meningosarcoma in particular, as outlined by Hsü, is given.

3. A clinical summary with report of autopsy in a case of meningosarcoma with metastasis to the lung (the second case of the kind to be reported) is presented.

4. On the basis of the clinical history, the histopathologic features of the tumor and its invasive nature, it is concluded that the tumor is a fibrosarcoma of leptomeningeal origin with pulmonary metastasis.

Veterans Hospital.

16. Ewing, J.: Neoplastic Diseases, ed. 4, Philadelphia, W. B. Saunders Company, 1940, pp. 883-885.

News and Comment

VETERANS ADMINISTRATION RESIDENCY TRAINING PROGRAM IN NEUROLOGY

An additional residency training program for physicians desiring to train in neurology under the Veterans Administration has been organized by the Philadelphia Deans Committee. This residency covers a period of three years or less, depending on the previous experience of an applicant, and is designed to prepare residents for certification in neurology for the American Board of Psychiatry and Neurology. The program includes rotation through the Veterans Administration Hospital, Coatesville, Pa., Veterans Administration Regional Office, Philadelphia, and the Philadelphia General Hospital. Applications should be sent to the Manager, Veterans Administration Hospital, Coatesville, Pa.

MEDICAL SECTION OF AMERICAN SOCIETY FOR PSYCHICAL RESEARGH

A group of physician members of the American Society for Psychical Research has organized a medical section to investigate the psychiatric and psychoanalytic aspects of telepathy and related phenomena. Recent publications in the various psychiatric journals bear witness to the growing importance of this subject to all those engaged in personality studies, as well as in psychotherapy.

Further information as to the aims and purposes of this section, and its program, can be obtained from the executive secretary, Mrs. L. A. Dale, Suite 1A, 880 Fifth Avenue, New York 21.

ASSOCIATION FOR PHYSICAL AND MENTAL REHABILITATION CONVENTION IN MAY

The Association for Physical and Mental Rehabilitation will hold its third annual convention at the Hotel New Yorker, New York, May 18 to 21, 1949. More than 500 representatives from the nation's Veterans Administration, Army, Navy and civilian rehabilitation agencies will be present. Mr. Leo Berner, chief corrective therapist of the Bronx Veterans Hospital, is chairman for the convention.

RESIDENCIES IN NEUROPSYCHIATRY

Two approved one year residencies in neuropsychiatry at the Parkland Hospital, Southwestern Medical College, Dallas, Texas, are now available. The hospital, a teaching institution, has a thirty-two bed ward service. For further information, write the Department of Neuropsychiatry, 2211 Oak Lawn Avenue, Dallas, Texas.

RESIDENCIES IN NEUROLOGY UNDER VETERANS ADMINISTRATION

Residencies in neurology are now available under the Veterans Administration program, beginning Jan. 1, 1949, at the Bellevue Psychiatric Hospital, New York. Application may be made to Prof. S. Bernard Wortis.

Obituaries

PROFESSOR CLOVIS VINCENT

1879-1947

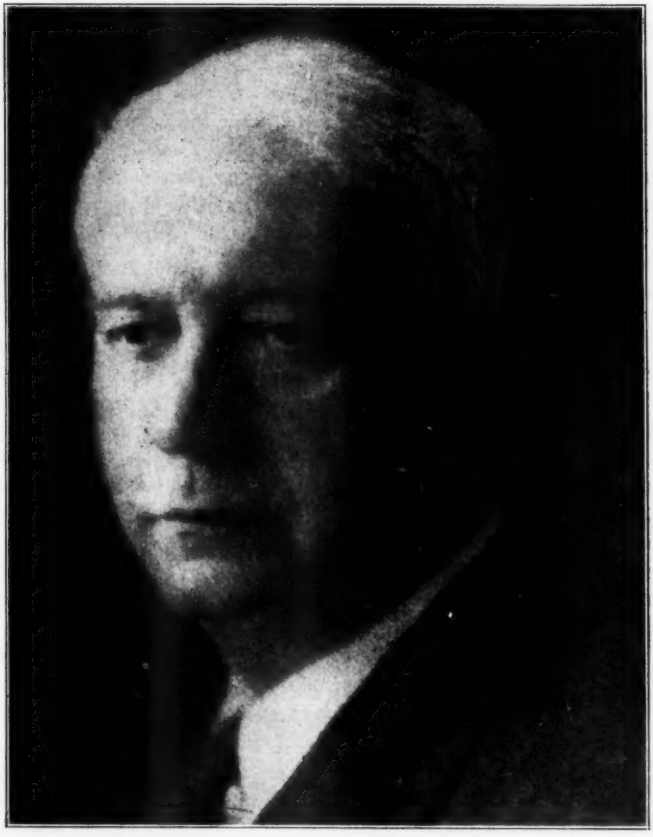
Last autumn in Paris, as the leaves were falling and the winter's gloom was closing on the city, the scalpel slipped from the failing fingers of my friend Clovis Vincent, and he reluctantly gave up the valiant struggle in which he had been engaged for the last twenty years. In 1929, at an age when others would have been thinking of peacefully enjoying a well earned professional eminence, he undertook, against overwhelming odds, an arduous campaign which he pursued, through war and peace, to a victorious conclusion. That struggle will be remembered as one of the epics of French medical history.

Clovis Vincent was born at Ingré (Loiret) on Sept. 26, 1879. Like Harvey Cushing, one of his heroes (the other was Babinski), whom he resembled astonishingly in many ways, he was the son and grandson of physicians. He prepared at Orléans, studied medicine in the city of Paris and served his internship in its hospitals, gaining the gold medal in 1909. Even before beginning his internship he had come under the influence of Babinski, whom he adored and whose method he adopted. He became hospital physician in 1913, a title essential for any medical man who wishes to have access, in Paris, to clinical material for study, and settled down as assistant to his master. Then came the first world war.

Vincent was mobilized throughout the duration of the war. His conduct during this time is legendary. In 1915, at the assault of Vauquois, he entered with the first assailants, gaining the military cross with palm. Later he won another palm and was made, because of his military exploits, commander of the Legion of Honor. In the intervals between his bouts of martial ardor he became chief of the neurologic center of the ninth region and finished the war as assistant to Babinski at the Pitié.

Following the example of his chief, he refused to go through all the wasted effort and political maneuvering necessary to advancement in the Parisian academic world and consecrated himself to the patient and controlled observation of neurologic phenomena. Soon they hearkened to his voice in the neurological society. It was there that I first saw him, in 1920. At that time he was very restless, almost choreic, but his discussions were acute and logical. I never came to know him

well in that period, for I was a pupil of Pierre Marie and my ideal of the Gaul was Charles Foix—*beau parleur, bon vivant et homme d'esprit* —it is impossible to describe him except in French—whose early death was an irreparable loss to neurology.



PROFESSOR CLOVIS VINCENT
1879-1947

During those years Vincent made important contributions to neurology. One might mention his studies of hysteria, nervous troubles of reflex or physiopathic nature, chronic syphilitic meningitis, epidemic encephalitis, pseudoparaplegias in flexion of cerebral origin, spinal compression and many others. Babinski cherished him and looked on him as a favorite disciple and designated successor.

In 1911 Babinski had made the diagnosis of a tumor of the spinal cord and had it removed by Lecène, the first operation of its kind in France. But he preferred to send his surgical cases to de Martel. The latter not only was a good surgeon but was also interested in surgery of the nervous system; perhaps there was some sympathy between them, for the young surgeon was also outside the regular academic tradition. When Babinski died in 1932, Vincent succeeded to his service at the Pitié and continued to send patients to de Martel for operation. The two had been intimate friends since their school days.

I next saw Vincent in Boston (1927), whither de Martel had lured him to present a decoration to Harvey Cushing. I stood with them in his parlor and translated their simple, but eloquent, eulogies. Next day Cushing was giving a clinic to the New England Pediatric Society. At first Vincent, understanding little, fidgeted in his seat, as usual. Suddenly he stopped, looked intently at the patient and whispered to de Martel. "Oh! that is a technical matter; leave that to me," answered the surgeon. "Yes, but you said I should come over here to see how the Americans operate on the brain. I want to know why these children do not have hernias in the cervical region." "Keep quiet and listen," said de Martel, "Ask Bailey about it afterward." Later I explained that de Martel, being a busy general surgeon, did not take time to sew the wound thoroughly. "Aha!" exclaimed Vincent, "I see." From then on he was as full of "insatiable curtiosity" as the elephant child.

As I foresaw, trouble was not long in coming. Of the clashing controversy which ensued I know only by hearsay, and I have heard of it at length from both of them. De Martel even came to Chicago to talk with me about it. Both suffered; they were proud and courageous men, and they loved each other. But Vincent had become convinced that de Martel would never take his responsibility seriously and was incapable of establishing modern neurologic surgery in France. So he withdrew from their partnership and began, as Babinski had previously urged him, to operate on his own patients, taking them from the Pitié to a private hospital and paying their expenses himself. This was a serious step; not only was it contrary to tradition in his city, but he was close to 50 years of age. He soon found that he needed more training, and one day I received a cablegram that he was on his way to my clinic with his two assistants—David and Puech.

The next three months were hectic. They were at my heels all day long, every day—questioning, arguing, gesticulating. I had scarcely time to eat and sleep. I taught them all I could, and was happy to do it, but I heaved a great sigh of relief when they left for Boston via Ann Arbor. Vincent never ceased to express his gratitude to me and Peet, but Cushing made a greater impression on him. They were kindred

spirits—the same inflexible courage, the same ruthless determination, the same disregard of others in the pursuit of their goal, the same devotion to their patients. Thereafter Vincent patterned his life after Cushing, as he had previously after Babinski. His home life practically ceased; he drove himself and his associates mercilessly.

Working, talking, intriguing for his purpose as he never would have done for himself, he succeeded in getting an operating room in his medical service at the Pitié. There he showed what he could do. Cushing watched him operate there and told me that the work was excellent. The same remark he made to Edouard Busch, of Copenhagen, perhaps to others. Vincent's success convinced Cushing that a man might enter neurologic surgery through neurology rather than general surgery. Even de Martel admitted that Vincent learned surgical technic quicker than it would have taken him to learn neurology. These remarks should not be interpreted as approval of Vincent's career as a model for the training of neurologic surgeons. Another man without his ability and emotional drive would have failed. And it should not be thought that Vincent simply began to operate without surgical training. He assisted de Martel for several years and, I am told, was even allowed to do appendectomies and hysterectomies as a means of training in dissection and suturing. He could not have succeeded without first mastering the fundamental principles and technics of surgery.

As a fitting tribute to his magnificent accomplishment, with the aid of the Rockefeller Foundation, a chair of neurosurgery was established in the university and Vincent was made professor. His inaugural lesson, given in the Great Amphitheatre of the Faculty on Jan. 26, 1939, was a masterpiece of modesty and devotion. It seemed that now he could settle down to develop a school of neurosurgeons for France. Then came another German invasion.

We know that his colleague and protagonist could not face the storm. Vincent merely worked harder than ever. He lived in the hospital and fought for his clinic, his patients and his work. I have not heard the story of those years from any one who lived through them with him. After the Germans had left, he received the resistance medal.

But he was worn out. His spirit had driven him beyond the strength of his body. One brief letter I had from him, and then silence. Now he is gone.

He established neurosurgery as a legitimate specialty in France. The position of neurosurgeon to the hospitals has been created. Petit-Dutaillis has been given the chair in the Faculty. This is a good choice, since he is in the legitimate academic tradition and is interested in the field; he will not betray Vincent's trust. And Vincent's pupil Puech has been made assistant professor. The future of neurosurgery in France is assured.

To the science of neurosurgery Vincent made noteworthy contributions in the midst of his struggles. He wrote an excellent account of optochiasmatic arachnoiditis, developed a method of total extirpation of cerebral abscess and of cerebellar tubercle and made original studies of cerebral edema and herniation. He had novel ideas also about the treatment of cerebral traumatism.

A gallant Gallic warrior in the struggle against disease has fallen; one who fought fair but asked no quarter and gave none. When Babinski was on his deathbed, he asked what would remain of him after his death. "At least the sign," said one of his pupils. "Yes," replied Babinski, "but that is not the best thing I have done. I showed the way to Martel and Vincent." And Vincent might have said, "I have fought the good fight. I have kept the faith. Neurosurgery is established in France." I am proud to have been his friend.

PERCIVAL BAILEY.

Abstracts from Current Literature

EDITED BY DR. BERNARD J. ALPERS

Anatomy and Embryology

THE HUMAN PYRAMIDAL TRACT: XV. A STUDY OF AXONS IN SELECTED CASES WITH CONGENITAL CEREBRAL MANIFESTATIONS. A. M. LASSEK, J. Comp. Neurol. **85**:477 (Dec.) 1946.

Lassek studied cross sections of the pyramidal tracts in 11 specimens of the medulla oblongata from brains of children and young persons who during life had practically complete paralysis of the motor system but exhibited intermittent convulsive seizures. Only the medullas, or parts of them, were available for the author's study. The tissues had been fixed in solution of formaldehyde U. S. P. for periods varying from a few days to five years. Microscopic sections of the medullas were stained for axis-cylinders by Bodian's technic or Davenport's silver nitrate method, and for myelin sheaths by the Weigert procedure. The pyramidal tracts were judged to be normal with respect to number and diameter of fibers in 10 cases. In the eleventh case the pyramids showed loss of some of the smaller fibers. This case was that of a child 7 years of age who had had meningitis at 7 months and whose cerebral cortex showed malformations in the cellular layers. The only possible variation from the normal which could be noted in the series was the relatively small area of the cross sections of the pyramids in some cases. However, the normal areas are not well enough known in the brain of the growing child to enable the author to say whether or not the small areas in the present cases were pathologic. The results of the study indicate that persistent and severe motor deficits can occur without destruction of the axons in the pyramids.

ADDISON, Philadelphia.

SENSORY GANGLION CELLS WITHIN THE CENTRAL CANAL OF THE HUMAN EMBRYONIC SPINAL CORD. TRYPHENA HUMPHREY, J. Comp. Neurol. **86**:1 (Feb.) 1947.

Humphrey examined 11 human embryos for the presence of nerve cells within the central canal of the spinal cord. The lengths of the embryos in which the cells were observed ranged from 5 to 37 mm., and their ages were estimated at 5 to 10 weeks. The cells were usually in clusters and were found oftenest at the caudal end of the cord. The largest number of cells noted in one embryo, and this was a 22.5 mm. embryo, was 76. The cells generally lie in the dorsal part of the central canal. These cells are considered sensory ganglion cells because of the similarity in size, shape and internal structure to the spinal ganglion cells. The fibers from the cell bodies within the central canal pass directly dorsad through the ependymal wall of the canal and the mantle layer into the marginal zone. In the mantle layer the fibers in some cases appeared to bifurcate, with one branch going rostrally and the other caudally. The inclusion of these cells within the central canal seems to occur during the closure of the neural folds. The sensory cells originate from the neural crest cells, which are themselves derived from the dorsalmost cells of the neural folds. If there is a lag in the separation of some of the neural crest cells, they may be carried within the closing neural tube.

The most frequent site of these cells is in the sacral region, and it is in this portion of the spinal cord that the occurrence of spina bifida and of dermoid cysts is most frequent. Disparities in developmental rates appear to be an important factor in the production of these several conditions. ADDISON, Philadelphia.

ISOLATION OF THE BRACHIAL SEGMENTS OF THE SPINAL CORD OF THE CHICK EMBRYO BY MEANS OF TANTALUM FOIL BLOCKS. VIKTOR HAMBURGER, J. Exper. Zool. **103**:113 (Oct.) 1946.

In order to block off the ingrowth of descending and ascending fibers into the brachial portion of the spinal cord, pieces of tantalum foil were inserted transversely in the cervical and thoracic levels of 2 and 3 day chick embryos. The embryos were fixed and sectioned five to six days after operation.

The pieces of tantalum foil were usually retained, and the tissues adjacent to the metal were in a healthy condition. The brachial portion of the cord was completely separated from the brain in 9 instances and from the caudal region in 2 instances. An almost complete separation occurred in 9 other cases, and in some of these only a few fibers connected the blind ends of the spinal cord.

Since cell counts of lateral motor neurons of brachial segments of the cord which were isolated from the brain or from both the cranial and the caudal region showed no difference between the isolated and the control cords, it is concluded that the differentiation of indifferent cells into motor cells proceeds normally in the absence of longitudinal fiber tracts.

The area of the gray matter of the isolated brachial segments of the cord measured almost the same as that of the control cords. Hence, proliferation of the brachial segments of the cord proceeds normally in the absence of longitudinal fiber tracts.

Most observations on the development of isolated regions of the spinal cord, both in chick and in amphibian embryos, agree with the author's findings that longitudinal fiber tracts are not necessary determining agents in the proliferation and differentiation of the cord. REID, New Brunswick, N. J.

CHANGES IN STRUCTURE AND THE KINETICS OF DIFFERENTIATING EMBRYONIC CELLS. JOHANNES HOLTFRETER, J. Morphol. **80**:57 (Jan.) 1947.

In this continuation of preceding studies on the structure and kinetics of embryonic amphibian cells, several cell species were isolated in vitro and examined with respect to the morphologic and kinetic changes occurring during their differentiation.

The cell membrane may be considered as the most active of the common structures of cells. Granulated endoplasm plays a more passive role, tending to preserve the cellular shapes created by the ameboid activity of the cell membrane. Migration of embryonic cells is due to rhythmic expansions and contractions of hyaline pseudopods, which develop mainly in the anterior portion of the cell. If the dragging posterior portion adheres to the substratum, it may be drawn out into a trailing process.

Large neuroblasts (Rohon-Beard cells) arising from the folds of the medullary plate can be compelled to leave the embryo by the application of a hypertonic standard salt solution. These are the first cells to adopt a specific shape. Mesectoderm cells can also be isolated by this method after closure of the neural tube. Neuroblasts, mesectoderm cells and leukocytes start with same architectural plan. The tapering pseudopods arising from their bulbous frontal portion move

like tentacles and take hold of a contact surface other than that to which the attenuated rear portion is attached. The arrangement, shape and migratory faculty of the various cell species are due to the local and temporal differences of cellular adhesiveness.

The behavior of ectoderm cells, mesenchyme cells and isolated myoblasts is also described in this article. REID, New Brunswick, N. J.

Physiology and Biochemistry

A STUDY OF SPASTICITY AND PARALYSIS. PHILIP F. WAGLEY, Bull. Johns Hopkins Hosp. **77**:218 (Sept.) 1945.

This study was undertaken in order to investigate the physiologic status of spasticity and paralysis in relation to the spinal cord. In so doing, consideration has been given in detail to the effects of lesions of the pyramidal tract and the spinal cord on skeletal muscle.

Seven monkeys (Macaca mulatta), ranging from 2 to 4 years of age, were used. In all instances, the operative approach was at the level of the laminas of the sixth and eighth thoracic vertebrae. In some instances the monkeys were operated on on several occasions. The animals were kept alive from twenty-one to nine hundred and sixty days and were examined repeatedly. The operative site and blocks from the cervical, thoracic, lumbar and sacral levels were cut serially and stained by the Marchi, Weigert, Bodian, Bielschowsky and Spielmeyer technics and by the Quigley-Smith modification of the Weigert method. Sections of the medulla and midbrain of 3 animals were stained by the Nissl method. By killing some of the animals three weeks after a second operation and staining the sections by Weigert and Marchi technics, the fibers cut at the first and second operations could be differentiated.

Wagley concludes as a result of this study that spasticity unassociated with paralysis can be produced by lesions in the spinal cord of Macaca mulatta. The interruption of the reticulospinal fibers seems to produce this group of symptoms. It is apparent that there is an intimate functional and anatomic relation between the corticofugal system from area 4 s and the reticulospinal tracts. The division of other spinal cord systems (such as the parietospinal, rubrospinal, vestibulospinal and spinocerebellar) in conjunction with that of the reticulospinal fibers prevents the appearance of spasticity. That their interruption by hemisection of the cord does not prevent the appearance of spasticity in man may signify an even greater importance of the reticulospinal system in the man than in the macaque.

Brisk tendon reflexes of low threshold were associated either with hypotonicity or with hypertonicity of the same muscles. The latter state of tone was always found with brisk tendon reflexes of low threshold. Interruption of the pyramidal tract severs fibers of multiple cortical origin and results in (1) impairment of phasic activity, (2) hypotonia of some muscles and (3) definite evidence of release. No pattern of anatomic segregation of corticospinal fibers (i. e., frontospinal and parietospinal) was found in the lateral funiculus.

As a general rule, the effectiveness of the function of a muscle made paretic by a lesion of the central nervous system increases progressively with the number of other muscles employed simultaneously and coordinately. Associated movements of an extremity depend on the integrity of the extrapyramidal fibers in the spinal cord. Their exaggeration follows isolated damage to the pyramidal tract. Atrophy of the proximal muscles is most marked following extrapyramidal lesions, that of the distal musculature following pyramidal lesions. Although a slight degree of

contracture results from pyramidal lesions, it is more intimately and extensively associated with extrapyramidal damage. Contracture occurs in both hypotonic and hypertonic muscles.

An increased briskness of adduction of the hallux on pinching the middle toe is the most reliable superficial reflex for the presence of isolated damage to the extrapyramidal fibers in the spinal cord.

Spastic paralysis follows division of two anatomically discrete systems. The paralysis appears after a lesion of the frontospinal tract (older usage, the corticospinal tract); the spasticity after interruption of extrapyramidal fibers, probably the 4 s tegmentum fibers, and/or the reticulospinal system.

GUTTMAN, Wilkes-Barre, Pa.

SUPPRESSION OF INSULIN SECRETION BY THE GROWTH HORMONE OF THE ANTERIOR PITUITARY AS DETERMINED WITH THE ISOLATED RAT PANCREAS IN A PERFUSION APPARATUS. E. ANDERSON and J. A. LONG, Endocrinology **40**:98, 1947.

Anderson and Long studied the direct effect of an extract of the anterior lobe of the pituitary on the insulin-producing cells of the pancreas. The extirpated rat pancreas was placed in a perfusion apparatus and subjected to the action of hormones of the anterior lobe of the pituitary gland; then the blood which had been circulated through the pancreas was assayed for insulin by injection into an adrenodemedullated, diabetic, hypophysectomized rat.

Under these conditions, the growth hormone of the anterior lobe of the pituitary gland does not stimulate the islets directly to secrete insulin. In studying the combined effects of growth hormone and hyperglycemia, it was found that the presence of the growth hormone prevented the secretion of insulin which would be expected to occur with an increase in blood sugar. If the growth hormone was inactivated, its inhibitory effect on secretion of insulin disappeared. Rat pituitary extract inhibits insulin secretion in the same way as the purified growth hormone. Neither thyroxin nor adrenal cortex extract inhibits the stimulating effect of hyperglycemia on insulin secretion. From this, the authors conclude that neither the thyrotropic nor the adrenocorticotropic hormone of the pituitary gland inhibits insulin secretion.

Anderson and Long conclude that the data presented do not support the concept of a pancreatotropic hormone of the pituitary gland; on the contrary, the anterior lobe of the pituitary contains a factor which inhibits insulin secretion.

FRANKEL, Philadelphia.

THE CLEAVAGE OF PHOSPHOLIPIDES BY BRAIN TISSUE. W. M. SPERRY, J. Biol. Chem. **170**:675, 1947.

Incubated homogenates of rat brain in either saline-carbonate buffer or the Krebs-Henseleit buffer without phosphorus contained less alcohol-ether-extractable phosphorus resulting from cleavage of phosphatides. Brains of young rats showed no more cleavage than those of old ones. Minced brain suspended in carbonate buffer behaved similarly.

PAGE, Cleveland.

TISSUE CULTURES OF THE BRAIN: INTERCELLULAR GRANULES. MARY JANE HOGUE, J. Comp. Neurol. **85**:519 (Dec.) 1946.

In the course of examining tissue cultures of brain cells grown in roller tubes, Hogue noted the presence of masses of fine granules between the intact cells. The granules were consistently present in cultures of the various parts of the brain of man and other mammals, both embryonic and mature, but were not observed in

cultures of other organs. The granules were seen in the cultures soon after they were made, especially along the cut edges of the explants. When the cultures were twenty-four hours old, cells singly or in groups were seen migrating through the masses of granules. The nerve cells as they passed beyond the massed granules often carried small groups of granules along with them. The granules stuck together and adhered to the cells even after the cells had wandered far from the explant. They adhered to the bodies of the cells and to their larger processes, but not to the actively moving tips of the processes. Examination of fresh brain tissue from animals recently killed showed cells with granular contents and also groups of granules not enclosed by visible cell membranes. Hogue concludes that the intercellular granules seen in young tissue cultures have been released from cells which have been injured and that those seen in old structures are the products of disintegration of the migrating nerve cells or their processes.

ADDISON, Philadelphia.

DECEREBRATE RIGIDITY. ARTHUR A. WARD JR., J. Neurophysiol. **10**:89 (March) 1947.

Ward produced decerebrate rigidity in cats and monkeys by intravenous injection of sodium cyanide. During the period of decerebration, the electrical activity disappeared in structures rostral to the midbrain, and the electrical activity of the suppressor region of the reticular formation of the bulb was decreased, whereas the activity of the facilitatory region in the lateral tegmentum of the pons was unchanged or increased. Ward advanced the hypothesis that sodium cyanide or lesions in the midbrain produce decerebrate rigidity by interrupting all afferent impulses to the suppressor region in the bulb, with resultant deprivation paralysis. The facilitatory region continues to receive afferent impulses for the nuclei of the cranial nerves and from the spinal cord, the facilitatory influence on the internuncial pools of the spinal cord being unaltered. Decerebrate rigidity is the outward manifestation of the deprivation paralysis of suppressor mechanisms and of continued, or even enhanced, activity of the facilitatory mechanism.

Ward found that the decerebrate state due to sodium cyanide can be modified by small lesions in the reticular formation of the brain stem, whereas lesions destroying the facilitatory region prevent the induction of decerebrate rigidity. Lesions in the reticular substance alone yield decerebrate rigidity.

FORSTER, Philadelphia.

CONVULSIVE ACTIVITY INDUCED BY FLUOROACETATE. ARTHUR A. WARD JR., J. Neurophysiol. **10**:105 (March) 1947.

Ward studied the electrical activity of the cortex and subcortical structures in cats and a monkey during seizures induced by injection of sodium fluoroacetate. During the repeated tonic seizures induced with fluoroacetate, there were local, rhythmic seizure discharges in subcortical structures. No clear correlation was found between the electrical activity of the cortex and the paroxysmal activity in the thalamus, hypothalamus or reticular formation of the pons. Dome and spike activity was recorded from the cortex synchronously with rapid seizure discharges in subcortical structures.

FORSTER, Philadelphia.

INJURY POTENTIALS ALONG PERIPHERAL NERVES IN RELATION TO HISTOLOGICAL STRUCTURE. BROR REXED, J. Neurophysiol. **10**:113 (March) 1947.

Rexed studied the injury potentials at various levels of peripheral nerves in the lumbosacral region of cats and found that the potentials diminished continuously from the spinal nerve roots toward the periphery. The proportion between the

injury potentials of the ventral roots and those of the tibial nerve was 4:1. This drop in injury potential was found to be related to the caliber of the nerve fibers at the various levels. A greater relative cross sectional area of a fiber corresponded with greater action potential.

FORSTER, Philadelphia.

EFFECT OF AFFERENT IMPULSES ON CORTICAL SUPPRESSOR AREAS. ERNST GELLHORN, J. Neurophysiol. **10**:125 (March) 1947.

Gellhorn studied the electrical activity of suppressor and sensory cortical areas. The initiation of afferent nociceptive impulses by electrical, chemical or mechanical stimulation increased the electrical activity of the suppressor as well as the sensorimotor and projection areas of the cortex. The responses were similar in both areas to threshold and to suprathreshold stimuli. The process of increased activity or excitation seems to be based on a diminished synchronization and on recruitment of additional neurons. The author suggests that the suppressor areas are involved in a homeostatic mechanism.

FORSTER, Philadelphia.

EFFECT OF REINNERVATION ON COLLAGEN FORMATION IN DEGENERATING SCIATIC NERVES OF RABBITS. M. ABERCROMBIE and M. L. JOHNSON, J. Neurol., Neurosurg. & Psychiat. **10**:89 (May) 1947.

Abercrombie and Johnson investigated the effect which reinnervation might have on formation of collagen. For this purpose, nonreinnervated sciatic nerves of rabbits following complete severance were compared with reinnervated nerves following crushing after one hundred days was allowed to elapse. The results showed no significant differences in collagen content in the two groups. The authors conclude, therefore, that collagen formation is uninfluenced by reinnervation. The wet weight and the noncollagen nitrogen were, however, higher in the reinnervated nerves, owing to the added material of the new nerve fibers. There was some evidence that the endoneurial fibroblasts, rather than the Schwann cells, were responsible for the formation of collagen. There were no signs of inhibition of fibrosis in the crushed nerve, as assumed by Weiss.

N. MALAMUD, San Francisco.

ANTICONVULSIVE ACTION OF BELLADONNA AND ATROPINE. S. OBRADOR, P. ORTIZ and J. MANDOKI, Bol. Inst. de estud. med. y biol. **3**:161 (Sept.-Dec.) 1945.

In 3 of 5 cats given intramuscular injections of 0.5 to 1 mg. of belladonna per kilogram of weight, there was an evident rise in the convulsive threshold; the convulsions were less intense after electrical stimulation. In 2 cases there were no changes in the convulsive threshold. In another series, of 5 cats, the convulsive threshold was studied after the injection of 1 to 2 mg. per kilogram of atropine intraperitoneally or intramuscularly. In 3 of these 5 animals, a definite rise in the convulsive threshold was also noted with diminution in severity of the seizures. In 4 cats the same experiment was repeated after cutting both vagus nerves in the neck and denervating the carotid sinuses. In 3 of these cats, there was a rise in the convulsive threshold, which was marked in 1 animal. In only 1 of 4 cats given intramuscular injections of scopolamine hydrobromide was there a mild elevation of the threshold; there were no changes in the others. Electroencephalographic studies before and after the intramuscular injection of hydrobromide in 2 epileptic patients showed no significant difference. One of the patients had frequent attacks during the period of administration of the scopolamine. The authors conclude that atropine and belladonna have a certain degree of anticonvulsive action

in some animals, probably central, and perhaps anticholinergic, since rises in the threshold were noted even after cutting of the vagus nerves and denervation of the carotid sinuses.

N. SAVITSKY, New York.

LIBERATION OF PHOSPHORUS FROM BRAIN OF DOGS STIMULATED BY CONVULSANT DRUGS. VINCENTE H. CICARDO, Publ. d. Centro de invest. tisiol. **9**:123 (June) 1945.

"Metrazol" and picrotoxin were used to induce convulsions in 22 dogs in which the spinal cord was destroyed. "Metrazol" was given in doses of 0.20 to 0.30 Gm. Specimens of blood were taken simultaneously from the venous sinus and the femoral artery and vein immediately after the attack and ten or fifteen minutes later. The average amount of phosphorus in the blood from the venous sinus before the injection of "metrazol" was 4.90 mg. per hundred cubic centimeters, and that in the femoral artery, 4.75 mg. Immediately after the attack, the value for the blood from the venous sinus was 5.47 mg., and that for the femoral artery 4.99 mg., per hundred cubic centimeters. Fifteen minutes later the phosphorus content was 5.33 mg. in blood from the cerebrum and 5.18 mg. in the peripheral circulation. The average increase in the amount of phosphorus after an attack was + 19 per cent.

In 8 animals who were given picrotoxin, the average for the blood from the cerebral venous sinus prior to administration of the drug was 5.24 mg. per hundred cubic centimeters and for the femoral artery 4.91 mg. After the injection of 5 to 10 mg. of picrotoxin, there was an increase in the venous sinus blood to 5.99 mg. and in the peripheral circulation to 5.44 mg. immediately after an attack and to 6.40 and 6.23 mg., respectively, fifteen minutes later. The average increase was + 26 per cent. In 10 animals which were curarized there was no significant difference in the amount of phosphorus in the venous sinus after attacks induced by the administration of picrotoxin or "metrazol," probably because of a central action of curare.

N. SAVITSKY, New York.

Psychiatry and Psychopathology

PSYCHIATRIC PROBLEMS ON A SOUTH PACIFIC ISLAND. SAMUEL BURACK, Am. J. Psychiat. **101**:606 (March) 1945.

Burack made a two year survey of the psychiatric problems, exclusive of combat anxiety states, in a hospital on an isolated South Pacific island.

During the first six months on the island, the admissions for neuropsychiatric conditions from an infantry division were low, neurasthenic syndromes being mostly encountered. In the second six months, a definite increase in the neuropsychiatric cases and admissions to the hospital was seen. When the division moved to the combat zone, there was an immediate elimination of the cases of anxiety states and mental deficiency. At the end of the eighteen month period there was a gradual increase in the psychiatric admissions presenting rehabilitation problems. In this period it was observed that gastrointestinal disorders were prevalent and cases of neurocirculatory asthenia were increased.

After a twenty month period on the island, there was a pronounced drop in the number of neuropsychiatric cases. Burack attributed this to a policy of rotation which brought the patients back home. The reason stated was that the patient would rather keep his neurotic complaints and return home than be sent home with a neuropsychiatric disability. Consequently, four months after the rotation policy the admissions for neuropsychiatric disorders were at a low level, with improvement in morale.

Of the South Pacific diseases, malaria and filariasis, with their manifestations, contributed much to the production of neurasthenic and hypochondriacal syndromes.

Burack concluded that men should not be kept on an isolated island for more than six months, his reason being that the monotonous type of life affects the latent neurasthenic symptoms, and that longer periods are detrimental because they lead to introspection and hypochondriasis.

BORKOWSKI, Boston.

THE NEW ROLE OF PSYCHOLOGICAL TESTING IN PSYCHIATRY. K. MENNINGER, D. RAPAPORT and R. SCHAFER, Am. J. Psychiat. **103**:473, 1947.

The authors state that psychologic achievements, developmental, comparative and theoretic, have set at least a base line against which the evaluation of efficiency of function can be made. Diagnostic testing can now help to answer the question as to which psychologic functions are selectively impaired in different mental disorders and can serve to establish the presence or absence of the primary symptoms of mental disorder before the gross secondary symptoms are clinically conspicuous.

A variety of new intelligence, concept formation and projective tests are now available. These serve to elucidate assets and impairments in various psychologic functions.

The psychologic examiner should have knowledge of the dynamic etiology of the mental disorder as productive of specific defenses or their breakdown and theoretic knowledge of the psychologic functions which are related to these defenses or their breakdown, as well as knowledge of tests of psychologic functioning.

The systematic and intelligent use of psychologic tests in psychiatry should lead to a greater portion of correct and timely diagnoses. In addition, the tests may be utilized experimentally to investigate the nature of human thinking. By detecting potential or "latent" cases of mental disorders, such as schizophrenia, not as yet recognizable clinically, treatment may be instituted earlier and more specifically.

FRANKEL, Philadelphia.

PSYCHOANALYTIC OBSERVATIONS ON DREAMS AND PSYCHOSOMATIC REACTIONS IN RESPONSE TO HYPNOTICS AND ANAESTHETICS. BELA MITTELMANN, Psychoanalyt. Quart. **14**:498, 1945.

Mittlemann reports observations on 2 patients—one, a man who often took 3 grains (0.19 Gm.) of sodium amytal for attacks of dyspnea; the other, a woman who was given nitrous oxide as a dental anesthetic on five occasions. Both patients were given psychoanalysis. Sodium amytal, taken as a sedative, usually caused a decrease in anxiety and ensuing sleep. On each of the five occasions that the second patient received nitrous oxide anesthesia she had a dream. In these dreams the consistent elements reflected the patient's struggle against the loss of her faculties of perception and mastery. The changes in dream content, emotional tone and psychosomatic accompaniments (laughter, weeping and vomiting) varied with the dominant emotional constellation of the patient: She experienced general distress and depression with some anxiety when her problems were directly in evidence; detachment and amusement when she reacted with aloof, facetious contempt, and literary pleasure and splendor with mild elation when she attempted self magnification and fusion with the world. She reacted with laughter to aloof facetiousness, with weeping to sorrow over her pathetic state and with vomiting to disgust. The dental surgery activated unconscious fantasies of genital injury and their concomitant attitudes, all of which were expressed in her dreams.

PEARSON, Philadelphia.

ANALYSIS OF THE INFLUENCE OF ALCOHOL ON EXPERIMENTAL NEUROSES IN CATS. JULES H. MASSERMAN and K. S. YUM, Psychosom. Med. **8**:36 (Jan.-Feb.) 1946.

Masserman and Yum taught 21 cats to obtain food by opening a box, then to respond to various conditional signals and, finally, to solve difficult problems involving the passage of barriers and the manipulation of switches to secure their food. Alcoholic intoxication disintegrated their adaptive patterns to a varying degree. The most complex and recently learned patterns were particularly affected. Normal animals, however, showed complete restitution of function on recovery from intoxication, little habituation to alcohol and no consistent signs of acquiring a preference for alcohol.

Motivational conflicts between hunger and fear were then induced in the animals by special experimental procedures. These "experimental neuroses" were characterized by pervasive inhibitions of normal goal responses, hypersensitivities and aversions to stimuli associated with the conflictual field, loss of group dominance and marked and persistent aberrations of somatic and motor function. Small doses of alcohol disintegrated the relatively complex "neurotic" patterns and permitted relatively simple goal-oriented responses to supervene. A significant number of these "neurotic" animals acquired a definite preference for alcoholic beverages. However, as their reexploratory behavior while mildly intoxicated partially resolved conflicts, this addiction diminished, until nearly normal food choices were restored.

WERMUTH, Philadelphia.

SPONTANEOUS NEUROSIS IN CHIMPANZEES: THEORETICAL RELATIONS WITH CLINICAL AND EXPERIMENTAL PHENOMENA. D. O. HEBB, Psychosom. Med. **9**:3, 1947.

Hebb describes 2 cases of apparent neurosis in chimpanzees. The author believes that the disturbances in these animals cannot be attributed to any specific experiences.

The first animal, Alpha, a 15 year old female chimpanzee, had apparently been normal until the age of 12, when she suddenly began to refuse all solid food. Four months later, she lost her fear of food and began to avoid her attendant. After eight days, she stopped avoiding her attendant, but the fear of food returned. After repetitions of this cycle, she again became friendly to her attendant, and the fear of food gradually disappeared. Three years after the onset there was a repetition of the food-taking disturbance, which cleared up quickly.

The second animal, Kambi, a 16 year old female chimpanzee, had a previous history of instability. Morphine addiction was briefly established at the age of 8. Sexual activity was nonexistent before and after spaying, at the age of 12. Before adolescence, there were repeated episodes of depression and euphoria. During and after adolescence, the fluctuations of mood were less frequent, but more marked, with the depressive element predominating.

The author discusses human neuroses in an attempt to find criteria in them by which to test whether behavior in animals is neurotic. He lists six criteria which he considers constant features in recognizing human neuroses. He states that empirically human neurosis is a state which is (*a*) evaluationally abnormal, what people tend to avoid in themselves or to change in others; (*b*) emotional, arising from emotional conflict or disturbance; (*c*) generalized, tending to be manifested in a number of ways, not a response to a specific excitant; (*d*) persistent or chronic in some degree; (*e*) statistically relatively infrequent, and (*f*) not due to a specific

gross neural lesion. He concludes that the behavioral disturbances described in Alpha and Kambi meet the requirements for identifying neurosis as far as can be possible in the absence of verbal examination.

The author also applies these criteria to a critique of experimental neurosis. He advances a hypothesis about the underlying processes of neurosis based on an analysis of fear in man and in the chimpanzee. The key assumption of the hypothesis is that the integration of ordinary unemotional behavior depends fully on a precise timing of the cellular firing in the corticodiencephalic system, and that coordination in the firing of independent cells is to a great extent determined by experience. Disruption of functional organization involving the cortex might then result from (1) the simultaneous occurrence of processes which do not reenforce each other's affects (conflict), (2) the absence of afferent excitations which are essential to the maintenance of precise timing of neuronal activities and (3) metabolic disturbance, which changes the rate of firing of individual cells and thus changes their relationships to other cells. FRANKEL, Philadelphia.

CONFUSION DUE TO SUPPURATING HYDATID CYST OF THE LIVER. J. M. OBARRIO and J. M. OBARRIO JR., Prensa méd. argent. **33**:2571 (Dec. 27) 1946.

The authors report the case of a woman who was admitted in a state of delirium because of cholecystitis due to calculi. The onset was apparently sudden, with psychomotor restlessness, confusion and auditory and visual hallucinations. The hallucinatory experiences were terrifying and were accompanied with severe anxiety; they were more pronounced at night, and zoopsias were often present. Sleep was poor. The delirious state persisted and was followed by intense pain in the right upper abdominal quadrant; this was relieved by the application of an ice bag. The liver was enlarged, and a tumor could be palpated on the hepatic edge. Operation showed an infected hydatid cyst of the liver. After the operation, the temperature fell, and the mental disturbance became less severe; confusion and delirium persisted about ten days. The authors state that the cause of the mental changes was the suppurating hydatid cyst of the liver. There was no other evident cause for this mental disorder, which was of toxic and infectious nature. The patient's improvement following the removal of the focus of infection is in favor of this explanation. The authors were unable to find a similar case in the literature available to them. N. SAVITSKY, New York.

Meninges and Blood Vessels

BUBONIC PLAGUE MENINGITIS. E. G. H. KOENIGSFELD and K. P. S. NAMBIAR, Indian M. Gaz. **81**:474 (Nov.) 1946.

Koenigsfeld and Nambiar report 2 cases of plague meningitis which they observed in a series of 41 cases of bubonic plague. Diagnosis of plague meningitis was confirmed in a woman aged 47 by the detection of Pasteurella pestis in a culture of the lumbar puncture fluid obtained on the day before death. Lumbar puncture was not performed on a girl aged 7, and the diagnosis was made on clinical grounds. The symptoms were due to meningitis. Retraction of the head and opisthotonos indicated severe meningeal irritation, which, in the opinion of the authors, could be explained only by an acute breakdown of the blood–cerebrospinal fluid barrier, if not for the Pasteurella itself, at least for the toxins. In both cases the meningeal signs occurred after initial improvement. Both patients seemed to respond favorably to sulfonamide drugs and died at a comparatively late stage of

the disease. Sulfadiazine probably lessened the virulence of the germ without rendering it entirely harmless, with the effect that the disease took a more chronic course and meningitis had time to develop. If this conclusion is correct, more cases of plague meningitis may be observed in the near future, as sulfonamide drugs are now in general use in the treatment of plague. J. A. M. A.

RELATIONSHIP OF BENIGN LYMPHOCYTIC MENINGITIS AND GLANDULAR FEVER. HENRY TIDY, Lancet **2**:819 (Dec. 7) 1946.

The original description of glandular fever (infectious mononucleosis) by Pfeiffer in 1889 and that of benign lymphocytic meningitis by Wallgren in 1925 have little in common. The former was an acute infectious disease in children characterized by rapid, painless swelling of the cervical glands, slight constitutional symptoms, short course and favorable prognosis. The latter had acute onset with meningeal symptoms, characteristic cerebrospinal fluid findings, short mild course and no complications. In 1931, however, several writers described neurologic complications in glandular fever which are identical with the findings in benign lymphocytic meningitis, and the author raises the question whether every published case of benign lymphocytic meningitis may have been one of glandular fever; there is no evidence to exclude the possibility. He cites several cases of glandular fever with neurologic complications from the literature, in which the following general picture is presented:

1. The symptoms are most commonly meningeal but may involve any other portion of the central nervous system, or even the peripheral nerves. 2. The neurologic symptoms may develop together with, before or after the features of glandular fever. 3. The common characteristics of glandular fever tend to be slight in these cases. 4. In the early stages the blood count may be normal or a definite polymorphonuclear leukocytosis be present. 5. The changes in the cerebrospinal fluid are identical with those in benign lymphocytic meningitis.

The author states that the differential diagnosis rests on repeated and specific examinations for glandular fever. MADOW, Philadelphia.

MENINGITIS LEPTOSPIROSA. E. M. BUZZARD and J. A. H. WYLIE, Lancet **2**:417 (Sept. 20) 1947.

Buzzard and Wylie report 5 cases of Weil's disease (spirochetal jaundice) occurring in male patients from 9 to 23 years of age, manifested primarily as benign meningitis. All the patients had a history of contact with rats or their excreta, either through bathing in the river or through exposure in an occupational location. The chief symptoms were headache, fever, vomiting and photophobia. There was intense suffusion of the conjunctivas, and suffusion of the optic fundus was noted in 2 patients. Slight rigidity of the neck was present, and reflexes were not elicited in the arms and legs in the more severely ill. The cerebrospinal fluid was under slightly raised pressure and contained 50 to 300 cells, predominantly lymphocytes, per cubic millimeter. Agglutination tests of the blood for Leptospira icterohemorrhagiae gave positive reactions in concentrations of 1:10 at the end of the first week and of 1:10,000 in the third week. Although symptoms were moderately severe, at no time were the patients seriously ill, and all recovered completely without specific treatment of any kind. The authors suggest that leptospiras may gain access to the blood stream via the conjunctiva, nasal mucosa and fauces in bathing and that such an entry may predispose to the meningeal form of the disease.

MADOW, Philadelphia.

MENINGOENCEPHALITIS COMPLICATING GERMAN MEASLES [RUBELLA]. P. EFRATI, Harefuah **31**:193 (Dec. 1) 1946.

Rubella developed in a 22 year old man two weeks prior to admission to the hospital. Three or four days after the rash disappeared the temperature rose again; and headache, nausea and vomiting appeared. A week later there were signs of meningeal irritation. A lumbar puncture showed 1,689 cells per cubic millimeter, of which 95 per cent were lymphocytes. A culture of the spinal fluid was sterile. The patient's condition cleared up quickly, without complications.

N. SAVITSKY, New York.

Diseases of the Brain

KERNICTERUS: A FOLLOW-UP STUDY OF THIRTY-FIVE ERYTHROBLASTOTIC INFANTS. R. STILLER, Am. J. Dis. Child. **73**:651 (June) 1947.

Stiller studied the hospital records of 35 children with erythroblastosis in which there was the typical pattern of an Rh-positive child born of an Rh-negative mother, with the presenting complaint of either neonatal jaundice or anemia. Postmortem examinations were obtained on 5 of the 6 children who died. Two of the 6 infants showed signs of cerebral involvement related to kernicterus. At autopsy, the brain of the first child revealed areas of yellow pigmentation scattered throughout the cortex and the brain stem; on fixation, yellow and yellow-green pigment was seen, chiefly in the brain stem; staining of the basal ganglia was not noted. In the brain of the second infant there were areas of localized pigmentation in the floor of the fourth ventricle and in the insula. In a third child, who had opisthotonos, spasticity on the right and deviation of the jaw to the right, autopsy revealed a normal brain except for generalized engorgement of the cerebral vessels. Four of the 29 patients who are living have failed to develop normally and show signs of involvement of the central nervous system. They are thought by the author to have kernicterus. The author believes that transfusion therapy should be directed against the anemia, but that it is of no value in ameliorating the damage to the brain which has already occurred.

FRANKEL, Philadelphia.

HEREDITARY NYSTAGMUS OCCURRING AS SEX LINKED CHARACTER RECESSIVE IN FEMALE. C. W. RUCKER, Am. J. Ophth. **29**:1534 (Dec.) 1946.

According to Rucker, hereditary nystagmus appears as a constant, horizontal, to and fro movement of the eyes, pendular in type, or of small excursion on forward gaze and coarser on looking to the sides. Nystagmus is said to be inherited in any one of several different ways—as a mendelian dominant or recessive character, or as a sex-linked character. The propositus of the family reviewed in this report was a 7 year old boy whose father brought him to the clinic to have an operation performed on his eyes to steady them. The family had 231 members in six generations. The 21 members who had nystagmus were males, and all inherited it through females who themselves were not affected. In a number of instances the gene passed through a chain of several females before it became evident in a male descendant. In no case has a male transmitted the defect to his son. All descendants of nonaffected males are free from the defect. In this family the character is sex linked and without exception has been recessive in the females.

J. A. M. A.

IVORY VERTEBRA ASSOCIATED WITH LIPOMA OF THE SPINAL CORD. SAMUEL L. MELTZER, Am. J. Roentgenol. **57**:741 (June) 1947.

Among reported causative factors in production of a single "ivory" vertebra are myelogenous leukemia, tuberculous spondylitis, osteitis deformans, osteoplastic

metastases and Hodgkin's disease. Meltzer reports the case of a white man aged 33 with backache for sixteen years. The pain, which developed after a fall, had become considerably severer in the two years before study and was associated with a 20 pound (9.1 Kg.) loss of weight and increasing weakness of the legs. Neurologic examination revealed evidence of a lesion of the cord involving the fourth and fifth thoracic dermatomes. Roentgenograms of the cervical portion of the spine demonstrated a diffuse, but conspicuous, increase in density of the posterior portions of the bodies of the sixth and seventh cervical vertebrae and their laminas and spinous processes. Cervical myelograms showed an irregular defect on the left side from the fifth cervical to the first thoracic segment.

At operation a large, irregular lipoma was observed occupying the left side of the lower cervical portion of the cord. The pathologic report confirmed the diagnosis. Neurologically, the patient made practically a complete recovery after removal of the tumor.

TEPLICK, Philadelphia.

NEUROLOGIC MANIFESTATIONS IN PREICTERIC PHASE OF INFECTIOUS HEPATITIS. L. WEINSTEIN and W. T. DAVISON, Am. Practitioner **1**:191 (Dec.) 1946.

Weinstein and Davison describe 4 cases of infectious hepatitis with manifestations of severe involvement of the nervous system in the preicteric phase of the disease. Headache, rigidity of the neck, increase in the number of cells in the spinal fluid, pain in the eyes, photophobia, blurred vision, numbness of a hand, lethargy, a positive Kernig sign, hypoactive deep reflexes, absence of the superficial reflexes and paralyzed bladder were the symptoms presented by these patients. If the attacks occur during the time of the year when poliomyelitis is prevalent, as did the ones reported in this paper, a diagnosis of acute anterior poliomyelitis may be made. A history of contact with a case of infectious hepatitis may be helpful in suggesting this disease as the cause of the neurologic signs and symptoms. In cases of so-called nonicteric infectious hepatitis the cause of the neurologic signs may be completely overlooked unless chemical studies of the blood and urine are carried out.

J. A. M. A.

DIAGNOSIS OF POSTCONCUSSIONAL STATE. G. M. BECK, New York State J. Med. **46**:2642 (Dec. 1) 1946.

Beck hopes that the material he presents will help clarify the confused picture of the postconcussional reaction and differentiate between traumatic cerebral dysfunction and pure anxiety. Cases of 172 patients who experienced either a blast or a head injury were analyzed and compared with 50 cases of patients with nontraumatic anxiety. The characteristic symptoms in the postconcussional patients, in the order of frequency, were headache, unconsciousness, feeling of insecurity, emotionalism, vertigo, difficulty in thinking, difficulty in letter writing and anomia. The most prominent diagnostic physical defects were in relation to the eyes. These consisted of convergence defect, nystagmus, disturbed upward gaze, external ocular muscle imbalance and inequality of pupils. Eighty-four per cent of the postconcussional patients had at least one of these ocular signs. Real vertigo was frequent in the patient with a postconcussional reaction; it did not occur in the nonorganic, control, group. Word recall was the only test of the mental status, the results of which indicated a postconcussional reaction. Some of the previously forgotten events related to the injury were recalled by the postconcussional patients after "sodium amytal" narcosis.

J. A. M. A.

CAROTID BODY TUMOR IN ASSOCIATION WITH CAROTID SINUS SYNDROME. B. MCSWAIN, and F. C. SPENCER, Surgery **22**:222 (Aug.) 1947.

McSwain and Spencer report 2 cases of tumor of the carotid body. In the first case there was a history of episodes of loss of consciousness precipitated by rapid turning of the head and increased in frequency by wearing tight collars. A mass was palpable posterior and inferior to the left side of the mandible; after pressure on this mass, the patient became pale and lost consciousness, the blood pressure fell and the pulse decreased in rate. On release of pressure, the patient rapidly regained consciousness. Pressure on the right carotid sinus failed to affect the pulse or the blood pressure. In the second case there was a history of fainting after arising quickly or raising the head suddenly. In this case, also, a mass was felt posterior and inferior to the angle of the left side of the mandible, but pressure on this mass caused neither subjective manifestations nor change in pulse rate. Operation in each case revealed a hard mass at the bifurcation of the left common carotid artery which had invaded the surrounding structures. The microscopic observations in both these tumors were characteristic of tumor or adenoma of the carotid body.

FRANKEL, Philadelphia.

NEUROLOGICAL COMPLICATIONS IN ATYPICAL PNEUMONIA. J. MACDONALD HOLMES, Brit. M. J. **1**:218 (Feb. 8) 1947.

Holmes suggests that, although the neurologic complications of primary atypical pneumonia are rare, in many cases severe neurologic symptoms may overshadow an associated pulmonary infection unless a roentgenogram of the chest is made. Whereas the diagnosis of atypical pneumonia in such cases may have little therapeutic value, it may suggest a hopeful prognosis. Holmes thinks that the virus of atypical pneumonia is probably primarily viscerotropic and that when neural involvement does occur the results are not so severe as in infections with primarily neurotropic viruses; the tendency in such cases is toward complete recovery without sequelae. He describes 2 cases of acute infective polyneuritis, 2 cases of lymphocytic meningitis, 1 case of serous meningitis and 1 case of encephalitis, all associated with atypical pneumonia.

ECHOLS, New Orleans.

A MIDBRAIN SYNDROME FOLLOWING HEAD INJURY. MICHAEL KREMER, W. RITCHIE RUSSELL and G. E. SMYTH, J. Neurol., Neurosurg. & Psychiat. **10**:49 (May) 1947.

Kremer, Russell and Smyth report 9 cases of closed head injury which resulted in permanent motor disability attributed to damage of the midbrain. After the initial generalized signs had partially subsided, the following residual signs became established: (1) ataxia, in all but 1 case, predominantly unilateral and resembling to some extent the cerebellar type; (2) loss of balance and disturbances of gait, in 7 cases; (3) parkinsonian-like tremor, in 3 cases, resembling the tremor observed by Holmes with lesions of the tegmentum of the midbrain; (4) hypotonia, in 6 cases, usually limited to the side of severe ataxia; (5) signs of damage to the pyramidal tract of moderate degree, in all but 1 case, most apparent on the ataxic side; (6) sensory loss, in 1 case, and (7) oculomotor signs, in all cases, in the form of nuclear ophthalmoplegia, pupillary abnormalities, ptosis or retraction of the lid. The combination of these signs, particularly in the cases of unilateral involvement, pointed to lesions of the midbrain located in the superior cerebellar peduncle above its decussation, in the crus, red nucleus, substantia nigra, oculomotor nucleus and medial fillet. The location of the lesion was partly confirmed in 2 cases by pneumoencephalograms, which disclosed pronounced dilatation of the aqueduct of

Sylvius. The observations are in keeping with the frequent hemorrhagic lesions of the midbrain seen in rapidly fatal cases of head injury.

N. MALAMUD, San Francisco.

SURVEY OF RELATION BETWEEN EPILEPSY AND PREGNANCY. C. W. F. BURNETT, J. Obst. & Gynæc. Brit. Emp. **53**:539 (Dec.) 1946.

After a review of the literature on epilepsy that complicates pregnancy, labor, the puerperium or lactation, Burnett states that at the West Middlesex Hospital during the seven years from 1939 to 1945, inclusive, there have occurred 21 deliveries in 18 epileptic mothers. Records of 19 of the pregnancies, in 16 patients, have been available for analysis. In only 1 case was there a family history of epilepsy. Four cases of menstrual epilepsy were encountered, in 3 of which the epilepsy became worse during pregnancy. There were 2 cases of gestational epilepsy, in 1 of which the disorder began in the pregnancy under review and in 1 in a previous pregancy. There was a total of 8 cases in which epilepsy became worse during pregnancy. In 6 cases one or more signs of preeclamptic toxemia were present. There were no fits during labor, and none began during the puerperium. All infants were alive and healthy with the exception of 1 stillbirth. Breast feeding was allowed in 14 of the 18 cases, and it never aggravated the epilepsy. However, breast-fed babies tended to be sleepy if the mother received a sedative mixture containing bromides. The author presents 1 case of status epilepticus that occurred during pregnancy and in which termination of pregancy was successful. He advocates interruption of pregnancy as the method of choice in such cases.

J. A. M. A.

FINAL OBSERVATIONS ON CONGENITAL DEFECTS IN INFANTS FOLLOWING INFECTIOUS DISEASES DURING PREGNANCY, WITH SPECIAL REFERENCE TO RUBELLA. C. SWAN, A. L. TOSTEVIN and G. H. B. BLACK, M. J. Australia **2**:889 (Dec. 28) 1946.

Swan and his associates say that of 61 children comprising their first and second series they were able to reexamine 49. The most important result of the resurvey was the detection of 4 additional cases of deaf-mutism. In 1 patient spontaneous absorption of a cataractous lens had occurred. Many of the children were retarded in their physical development. A fourth series, consisting of 25 cases, was studied. In 17 instances (1 doubtful) the mother had contracted rubella in pregnancy. In 1 case the mother had suffered also from chickenpox. Fifteen of the babies born subsequently exhibited congenital defects. The abnormalities included cataract, deaf-mutism, heart disease, microcephaly, umbilical hernia, bifid uvula, mental deficiency, epilepsy, speech defect and concomitant strabismus. Thirteen of the 15 mothers had been ill with rubella during the first four months of pregnancy. The infants of 2 mothers, 1 of whom had had the disease in the first month and the other in the seventh month of gestation, were free from congenital malformations.

J. A. M. A.

Treatment, Neurosurgery

PENICILLIN IN THE TREATMENT OF NEUROSYPHILIS: I. ASYMPTOMATIC NEUROSYPHILIS. JOSEPH EARLE MOORE and CHARLES F. MOHR, Am. J. Syph., Gonor. & Ven. Dis. **30**:405 (Sept.) 1946.

Study of the effect of penicillin on various forms of neurosyphilis was begun at the Johns Hopkins Hospital in October 1943. Moore and Mohr report the

results of the first two years' experience with asymptomatic neurosyphilis. The patients included in this group had neither symptoms nor abnormal physical signs referable to the nervous system, but in each instance there was an abnormality of the spinal fluid. The cases are divided into those of early and those of late, asymptomatic, neurosyphilis. The division is arbitrary and is based on the duration of the syphilitic infection—less or more than four years.

A detailed presentation of the results of penicillin therapy on 48 patients with early, and 43 patients with late, asymptomatic, neurosyphilis followed for more than three months (average, nine months) after treatment is given.

The total dose of penicillin employed ranged experimentally from a minimum of 60,000 to a maximum of 6,000,000 units. The number of patients treated is too small to permit detailed analysis of results according to dose. In this study, reversal of the cerebrospinal fluid to normal was as readily accomplished with small as with large doses. As with the serologic reactions of the blood, time is required to produce normality of the spinal fluid. The data indicate clearly that penicillin exercises a favorable effect on abnormalities of the spinal fluid, affecting, in order, the cell count, the protein content, the colloidal gold test and the Wassermann reaction.

The rapidity and extent of the action of penicillin depends, on the one hand, on the degree of abnormality of the spinal fluid present before treatment and, on the other, on the duration of syphilitic infection. Allowing for the brief time limits of this study and the small number of cases involved, normality of the spinal fluid, once achieved, seems usually to be stable. GUTTMAN, Wilkes-Barre, Pa.

INTRATHECAL PENICILLIN IN BACTERIAL MENINGITIS. R. G. LIVINGSTONE and J. E. LEACH, Surgery **21**:683, 1947.

Livingstone and Leach report on the treatment with intrathecal injection of penicillin of 2 patients with streptococcic meningitis which developed as an acute postoperative complication of radical surgical procedures on the head.

The first patient, a white woman aged 59, began to show abnormal neurologic signs, tentatively diagnosed as encephalitis, three days after excision of recurrent carcinoma within the nasal cavity. Intramuscular injections of penicillin and oral use of sulfathiazole were instituted; later, sulfadiazine was substituted for the sulfathiazole. On the eighth postoperative day, clinical evidence of meningitis became apparent. Streptococcus viridans was obtained in pure culture from the spinal fluid. At this time, the dose of sodium penicillin was increased from 30,000 units every three hours to 80,000 units every four hours. Repeated transfusions of whole blood were given. Cultures of the spinal fluid repeatedly yielded pathogens. On the twenty-seventh postoperative day, 100,000 units of sodium penicillin in 5 cc. of spinal fluid was administered intrathecally. Four additional daily doses of 100,000 units of sodium penicillin were administered intrathecally. The patient had two generalized convulsions after the fourth intrathecal injection. The authors attribute this complication to the prolonged course of the meningitis, rather than to the possible toxic effect of the therapeutic agent. On the thirty-third postoperative day, the spinal fluid was sterile on culture and remained sterile subsequently. The patient was discharged as cured on the forty-first postoperative day.

The second patient, a white woman aged 58, was subjected to an extensive surgical procedure involving excision of the right side of the maxilla and exenteration of the right orbit. During this procedure the subarachnoid space was inadvertently entered. Treatment with intravenous injections of sulfadiazine, 2.5 Gm. twice daily, and intramuscular administration of sodium penicillin, 20,000

units every three hours, was immediately instituted. On the third postoperative day, when clinical evidence of meningitis appeared, 50,000 units of sodium penicillin in 5 cc. of isotonic sodium chloride solution U. S. P. was administered intrathecally, and the intramuscular dose of penicillin was increased to 50,000 units every three hours. Culture of the spinal fluid revealed Streptococcus hemolyticus (group A); 50,000 units of penicillin was administered intrathecally for seven days. No untoward reactions were noted. There was no growth on culture of the spinal fluid after the first examination. Clinical improvement was continuous, and the patient was discharged as cured on the twenty-eighth hospital day.

FRANKEL, Philadelphia.

HYPERTENSIVE HEADACHE TREATED WITH POTASSIUM THIOCYANATE. P. J. W. MILLS, Lancet **1**:324 (March 15) 1947.

Mills treated with potassium thiocyanate 27 patients who had benign hypertension with persistent headache and giddiness, carefully selected to exclude the functional element. One patient had complete relief; 21, much relief, and 5, only partial relief. Ten patients with rapidly progressive hypertensive vascular disease were also treated, and headache was relieved in those patients who had no rise in blood urea. Eight hypertensive patients with other symptoms, such as insomnia and tinnitus, were not relieved. The blood level was maintained at 5 to 8 mg. per hundred cubic centimeters. The mode of action of the drug in relieving headache is not known. There seems to be no definite relation between the lowering of the blood pressure and the relief of symptoms.

The author concludes that potassium thiocyanate has a definite, but limited, place in the treatment of hypertension and should be used if simpler forms of therapy do not afford relief. He states that it does not affect the course of the disease, but is purely palliative.

MADOW, Philadelphia.

Book Reviews

Ventriculocisternostomy: A Palliative Operation in Different Types of Non-Communicating Hydrocephalus. By Arne Torkildsen. Pp. 240. Oslo: Johan Grundt Tanum Forlag, 1947.

This recent, brief volume is a welcome addition to the series of technical monographs on neurosurgical procedures. Ten years ago, when Torkildsen conceived and carried out his first ventriculocisternostomy, no satisfactory solution had been found for the treatment of obstructive hydrocephalus. The best earlier palliative procedure had been Dandy's method of draining the dilated third ventricle into the cisterna interpeduncularis, behind, or the cisterna chiasmaticus, in front, whereby Stookey and Scarff, as well as White and Michelsen, had obtained a limited number of successful results. This operation, however, had its limitations, as it did not permit preliminary exploration of the posterior fossa. In cases of obstructing tumor at the base of the third ventricle, such as the craniopharyngioma, it could not be used at all.

Torkildsen's method of draining the dilated posterior horn of a lateral ventricle by means of a rubber catheter passed beneath the scalp, with its inferior end in the cisterna magna, has successfully solved these difficulties. One of the trephine openings made for the preliminary ventriculogram serves for insertion of the tube in the lateral ventricle, and as thorough an exploration of the posterior fossa as is desired can be made. Once it has been determined that there is no operable lesion, all that is necessary to secure permanent drainage around the obstruction is to pass a small rubber catheter between the galea and the occipital bone and to secure one end in the dilated lateral ventricle, the other in the cisterna magna. Care is necessary to assure that the upper end of the tube is patent within the ventricle and that the lower end is placed between the cerebellar tonsils and covered by reconstructed arachnoid of the cistern.

A priori, one might well have misgivings lest the lower end become occluded by arachnoidal adhesions and that in time the rubber tube might deteriorate. The author's ten year experience, with 32 cases, has demonstrated that these fears are groundless. Failure to release the blocked ventricular system occurred in only a single instance and was due to faulty insertion of the tube. Once drainage by-passing an obstruction was started, the tubes never showed any tendency to close; when they were examined after a period of years, there was no evidence that the rubber had deteriorated.

Torkildsen divides his cases of ventriculocisternostomy into three groups: group 1, 8 cases of tumor in the pineal region; group 2, 11 cases of tumor of the third ventricle or in its lateral walls, and group 3, 13 cases of benign atresia of the sylvian aqueduct. Considering the serious preoperative condition of many of his patients, the operative mortality was low, only 3 deaths occurring in the first two groups and 4 in group 3. Results in a large proportion of the survivors have been most gratifying. In the course of a few weeks after operation, the signs of intracranial hypertension disappeared, headaches and vomiting ceased and papilledema subsided. In the cases with obstruction caused by tumor, palliation was effective and often of long duration. Even in cases of gliomas of the brain stem survivals were recorded over periods up to four and three-quarters years, while in cases of pinealoma and craniopharyngioma, which, barring death from obstructive hydrocephalus, are slow to cause serious symptoms, many patients have continued to lead normal lives over periods ranging up to seven and a half years.

Results such as these are indeed impressive. Torkildsen advocates internal drainage of the ventricular system as the procedure of choice with pinealomas and craniopharyngiomas, once there is any evidence of obstruction to the outflow of cerebrospinal fluid. These tumors are known to grow slowly; their chief danger to life lies in the production of acute hydrocephalus, and the risk of direct attack is great. Furthermore, he argues logically that in the presence of hydrocephalus palliative drainage should be established first, even if direct attempts at later removal are contemplated. With the pinealomas, susceptible as they are to roentgen radiation, this should rarely be considered. With the cysts of Rathke's pouch, direct surgical evacuation will not be necessary unless the optic chiasm is compressed. Only in case of the benign colloid cysts of the third ventricle are most neurosurgeons in this country liable to disagree with the author's opinion and prefer a primary direct attack.

This monograph, of 240 pages, is a pleasure to read because of its clear style, good illustrations and extensive bibliography. The book begins with a good review of the anatomy of the ventricular-subarachnoid system, together with the production and absorption of cerebrospinal fluid. There is a critical review of past surgical attempts to relieve obstructive hydrocephalus and their failure often to benefit patients with benign lesions. It is clear that Torkildsen has devised a most successful solution of this problem, of which his well documented histories and long-observed cases give satisfactory proof. The personal experiences of the reviewer and a growing series of surgeons in this country have thoroughly corroborated his conclusions.

You and Psychiatry. By William C. Menninger, M.D., and Munro Leaf. Price, $2.50. Pp. 175. New York: Charles Scribner's Sons, 1948.

The authors have presented a reasonably short, concise and well written story of elementary psychodynamics from the psychoanalytic point of view. They have attempted, first, to present the neuroanatomic and neurophysiologic basis of nervous activity and to explain this in fairly simple language. The parental activities and the psychosexual development of the child are presented along classic lines, and then the conflict and its resolution through symptom formation are discussed. Most of the common mental mechanisms are presented. No technical language is omitted; but whenever such words are used they are immediately translated into everyday terminology, clarified sometimes by too homely examples.

The general tenor of the book is excellent. While it seems designed for lay persons, it must of necessity, through its choice of material, appeal most to a small fraction of them. It is ideally suited to medical students as an aid in their early orientation to psychiatry. All physicians would profit from reading this short manual.

The chapter on "If You Go to a Psychiatrist" deserves special mention for its good and wholesome presentation.

The Case Book of a Medical Psychologist. By Charles Berg, M.D. Price, $3.50. Pp. 260. New York: W. W. Norton & Company, 1948.

Dr. Berg has given a readable book, consisting of the verbatim reports of 25 cases during analytic treatment. Along with the productions of patients and therapeutists, he gives glimpses into technics of therapy, as well as his theories concerning the dynamics of the specific nervous illness under consideration.

Prefacing the case material, Dr. Berg discusses anxiety as the foundation of nervous illnesses. He states his theory of neuroses as the conflict resulting from

infantile instinctive impulses, which are prevented from reaching maturity by infantile morality or society. It should be noted that there is little digression from, or addition to, Freud's theories concerning the dynamics, structure and treatment of the neuroses.

The case material is well selected and representative of analytic practice. These cases illustrate a wide variety of psychopathology and dynamics. One can appreciate the direct simplicity of these presentations and discussions. Nowhere are there gaps in continuity in achieving this effect.

In striking contrast to the optimism expressed in the case records, the concluding chapter presents the author's feelings of hopelessness concerning man's ability ever to triumph over his instinctual destructive life forces. Dr. Berg, here, parallels the pessimism and resignation characteristic of Freud's work after the first world war. On the subject of prevention and cure, Dr. Berg states, "Instincts tend to cure themselves by gratification in one way or another. That is life. To try to cure them by any other means is working against nature." Again, in the same vein, "Life is fundamentally instinct-driven, the only permanent cure for it is death." Such an attitude is certainly in direct opposition to that motivating the large scale programs of preventive psychiatry going on throughout the world.

This book should be of clinical interest to psychiatrists, as well as those in the related professions which deal with emotionally disturbed people. It is a valuable addition to psychiatric literature and serves the needed purpose of helping to remove analysis and analytic technics from the aura and mystery which has surrounded them.